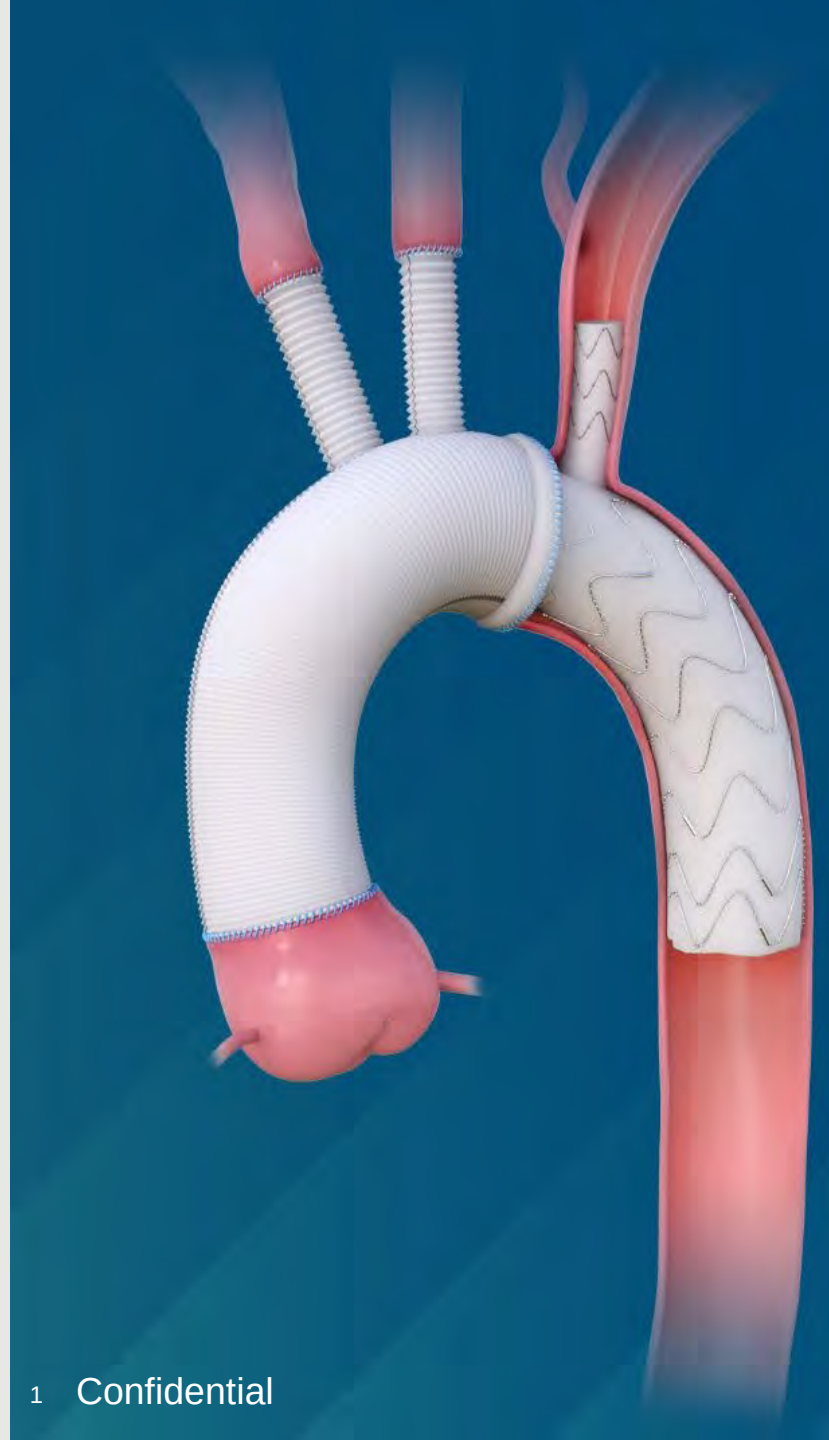


ARTIZEN

Investigator Meeting

ART2401.000-C

Version: 23Oct2025

ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Agenda

***Reminder:** All content shared in this meeting is considered confidential and should not be shared with anyone who is not affiliated with the study.*

Time	Section	Section Details	Presenter
8:00 – 8:10 am	Welcome	• Introductory comments	Pat Mackin
8:10 – 8:20 am	Meeting Objectives & Team Introductions	• Purpose, Team members, Study Partners	Erin Adams
8:20 – 8:35 am	Clinical Background	• Disease State, Standard of care, Unmet need	Dr. Marshall Stanton
8:35 – 9:35 am	Protocol Overview	• Study design, Schedule of activities, Endpoints, Data collection, Inclusion & exclusion criteria, Enrollment expectations, Benefits & risks, Q&A	Casey Jacketta
9:35 – 10:00 am	Eligibility Examples	• Presentation of 'test' patients	Stephanie Beall
10:00 – 10:10 am	Break		
10:10 – 10:40 am	Monitoring & Site Responsibilities	• Monitoring strategy, Visit schedule, Site responsibilities	Neoka Wofford
10:40 – 11:10 am	European Experience with E-vita OPEN NEO & EDE	• Review of E-vita OPEN NEO, Review of EDE, Review of B-SAFER data & experience, Lessons learned	Prof. Martin Grabenwöger, Dr. Eric Roselli
11:10 – 11:50 am	Device Training	• Device introduction, Deployment steps, Case review process, Case support	Don Jolley
11:50 – 12:20 pm	Hands on Device Training *(Investigators)*	• Investigator hands-on deployments	Don Jolley
11:50 – 12:20 pm	Site Team Breakout *(Site Staff)*	• Protocol deviations, Device storage, Product ordering & billing, Documenting early termination	Casey Jacketta, Alecia Charles
12:20 – 1:00pm	**Lunch**		
12:50 – 1:25 pm	Core Lab	• Access process, Upload instructions, Recommended imaging protocol, Definitions	Paul Bishop
1:25 – 2:00 pm	EDC	• Expectations for data entry, iMedNet review, Access instructions, eCRFs, Resources	Irene Lea
2:00 – 2:30 pm	Safety Processes	• Device deficiencies, SAEs, Events requiring adjudication	Stephanie Beall
2:30 – 2:50 pm	Steps to Activation & Timeline Review	• Requirements to activate, Timeline review, Planned analyses	Alecia Charles
2:50 – 3:05 pm	Questions?	• Open floor for questions	All
3:05 – 3:15 pm	Closing Remarks	• N/A	Dr. Eric Roselli, Dr. Marshall Stanton

0. Do you like Coca-Cola?

Company Overview

ARTIVION™ | **Arcevo™ LSA**
Hybrid Stent Graft System

ARTIVION

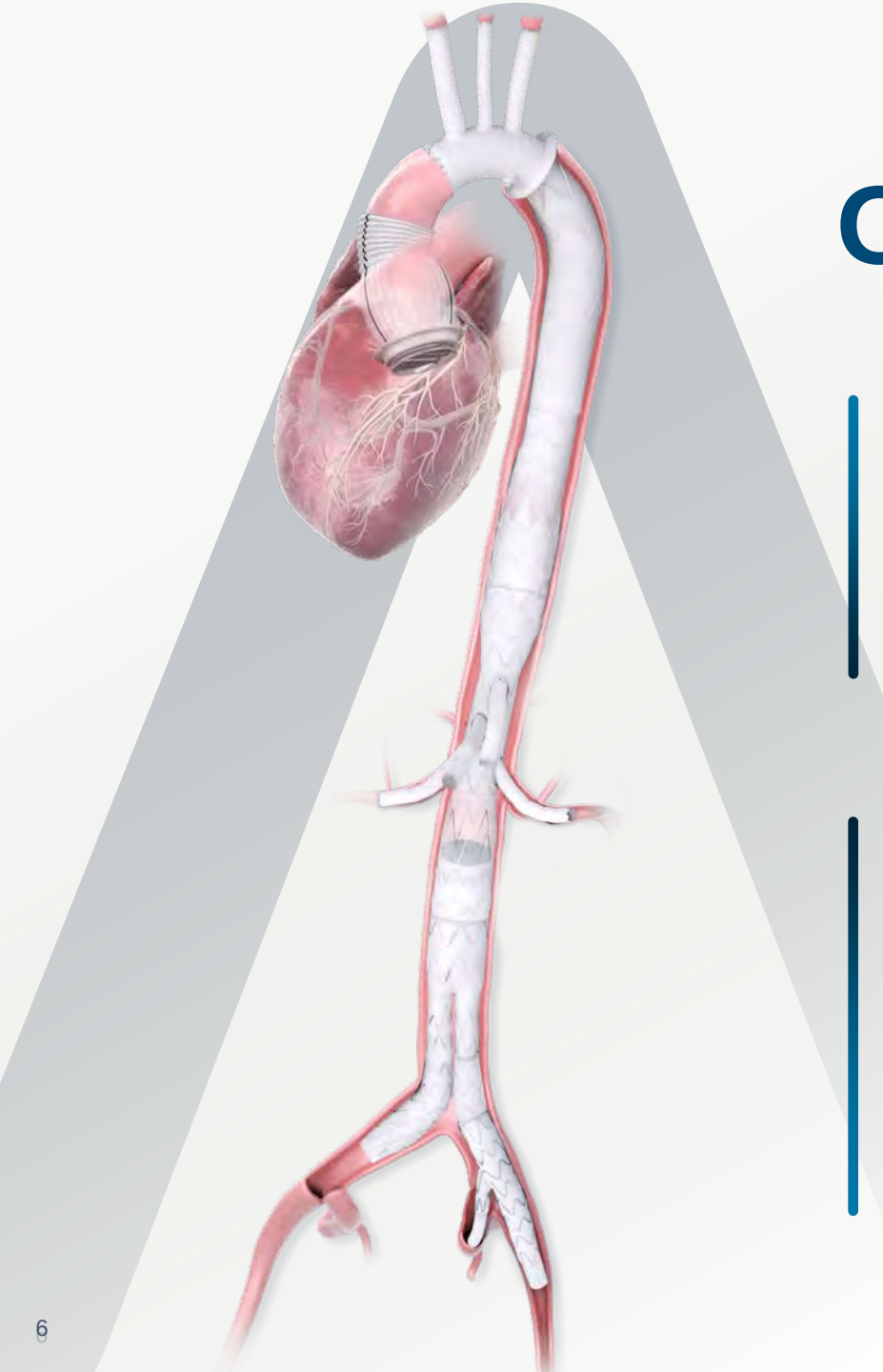
ARTIVION™

Aorta + Innovation + Vision

Artizen Investigators Meeting

October 23, 2025

Pat Mackin, CEO



OUR STRATEGY

WE WILL DELIVER

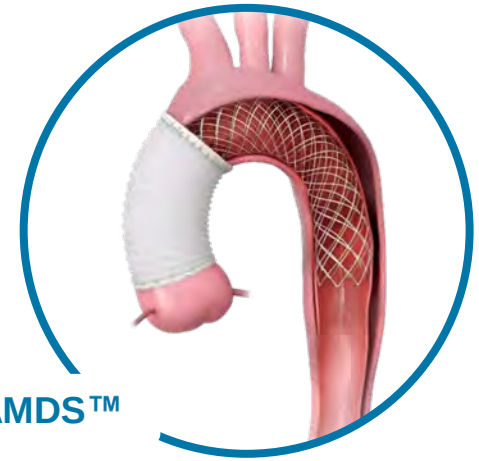
Double digit revenue growth by focusing globally on cardiac and vascular surgeons who treat patents with aortic disease.

WE WILL WIN

Through a deep understanding of our customer’s most significant clinical challenges and collaborating with them by developing or acquiring simple and elegant solutions that minimize these challenges and reduce healthcare costs.

AORTIC ARCH SOLUTIONS

Hybrid Dissection Prosthesis



AMDS™

Acute Debakey Type I (ADTI) With Malperfusion

Frozen Elephant Trunk Hybrid System

ARCEVO™ LSA

Dissections & Aneurysms

Endovascular Arch Branch System

NEXUS® ONE

Chronic Dissections & Aneurysms

AMDS is RX Only: Humanitarian Use Device. Authorized by Federal Law for use in the treatment of acute DeBakey Type I Aortic Dissection. The effectiveness of this device for this use has not been demonstrated. **NEXUS TRE™** NEXUS ONE™ is approved as an Investigational Device only and is not approved for commercial use in the United States.

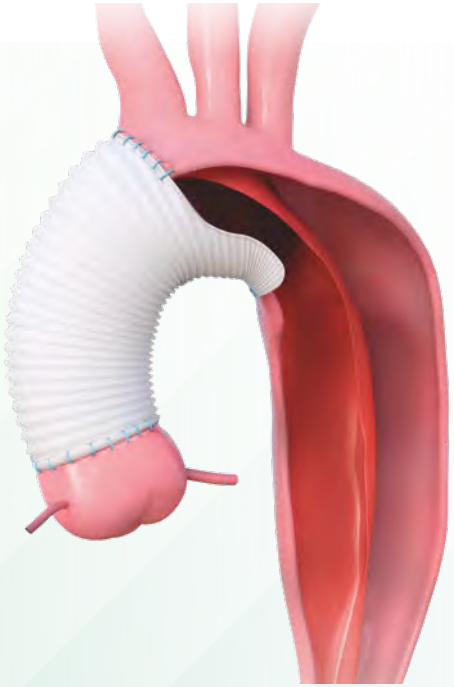
AMDS™ PERSEVERE US IDE STUDY

ARTIVION

Full IDE data demonstrates AMDS use significantly lowers 30-day Major Adverse Events (MAEs) compared to hemiarch control

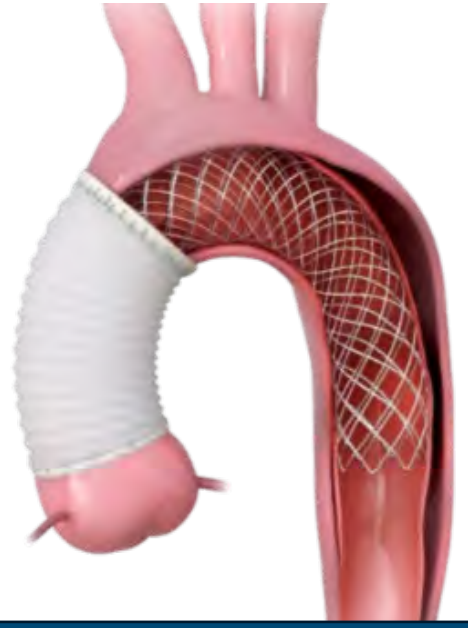
ACUTE DEBAKEY TYPE I (ADTI) WITH MALPERFUSION

Through Hospital Discharge Data



Hemiarch Reference Cohort Avg.[1] (n=790)		PERSEVERE[2] (n=93)
58.0%	≧ I MAE P<0.0001	26.8%
34.6%	All-Cause Mortality	9.7%
20.9%	New Disabling Stroke	10.8%
24.1%	Renal Failure Requiring Dialysis	19.4%
10.5%	Myocardial Infarction	0.0%
45.0%	Distal Anastomotic New Entry	0.0%

Full 30-Day Data



Total patients with ≧ 1MAE
PERSEVERE: 28%
Goal: < 40%

30-day data demonstrate AMDS induced positive aortic remodeling in over 80% of patients[3]

1. Zindovic I, 2019. Pacini D, 2013. Girdauskas E, 2009. Geirsson A, 2007. and Bossone E, 2002.
2. *Adjudicated data* as presented at STS January 2024, manuscript pending publication
3. *Adjudicated data* as presented at AATS April 2024, manuscript pending publication

EVOLUTION OF NEXUS

ARTIVION

NEXUS ONE™

NEXUS DUO™

NEXUS TRE™

2018 | 2019 | 2021 | 2023 | 2024 | 2025 | 2027

ENDOSPAN®

Exclusive Distribution Agreement

TRIOMPHE STUDY

1st Patient Enrolled

TRIOMPHE STUDY

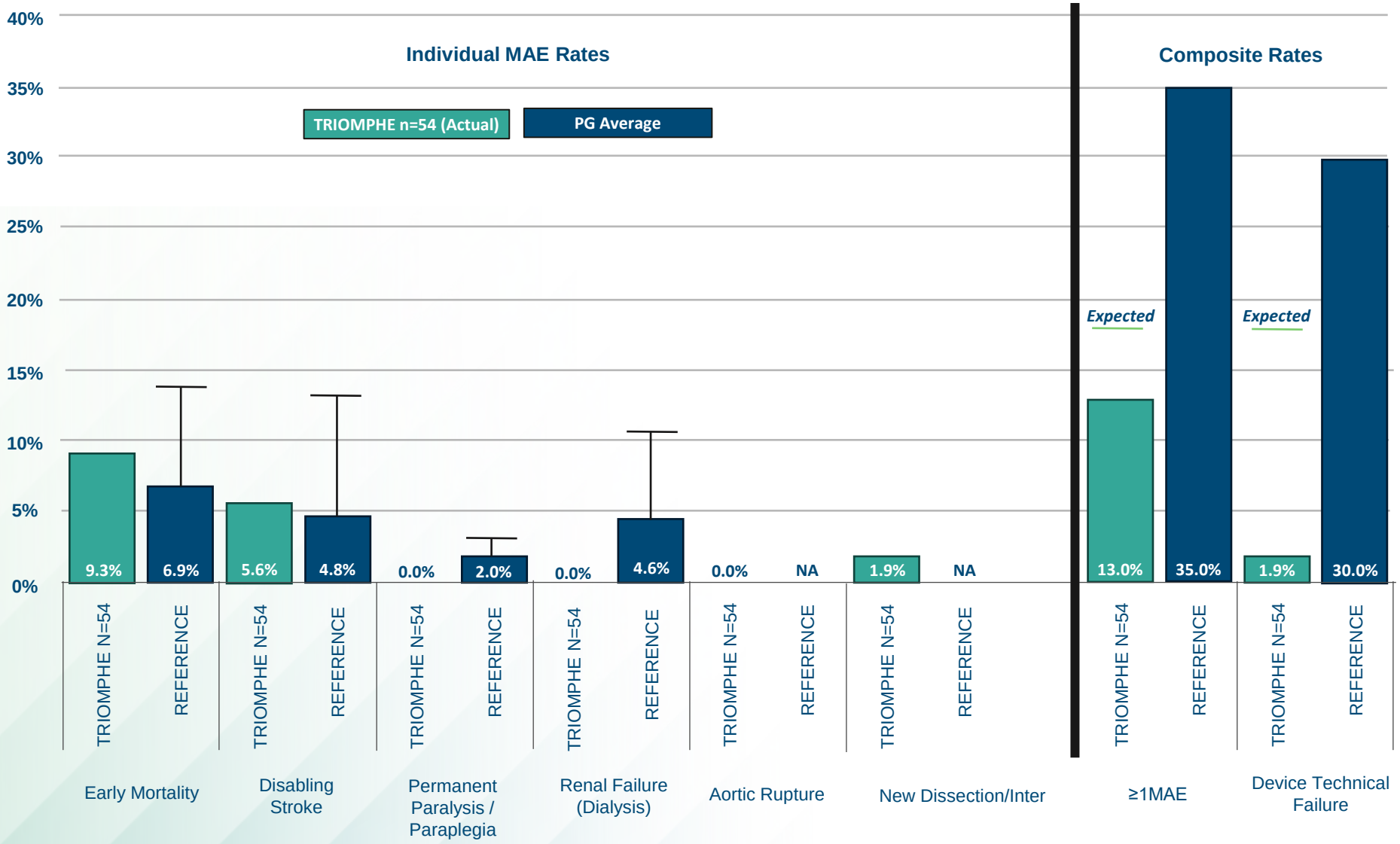
Enrollment Complete
Primary Arm (N=60)

FDA Approval
NEXUS® One

NEXUS TRE™ NEXUS ONE™ is approved as an Investigational Device only and is not approved for commercial use in the United States. NEXUS DUO™ and NEXUS TRE™ are custom-made devices based on the existing NEXUS ONE™, a CE-marked endovascular branch system for the aortic arch. The NEXUS is manufactured by Endospan Ltd. and distributed by Artivion. NEXUS is a registered trademark of Endospan Ltd.

NEXUS ® TRIOMPHE US IDE Trial Primary Endpoints

30-day primary endpoints



TRIOMPHE Protocol Hypothesis:

Device Technical Failure:
H_0: $P_t \geq 0.30$ vs. H_1: $P_t < 0.30$
Results:
1.9% (1/54), p-value <0.001
95% CI: 0.05, 9.89

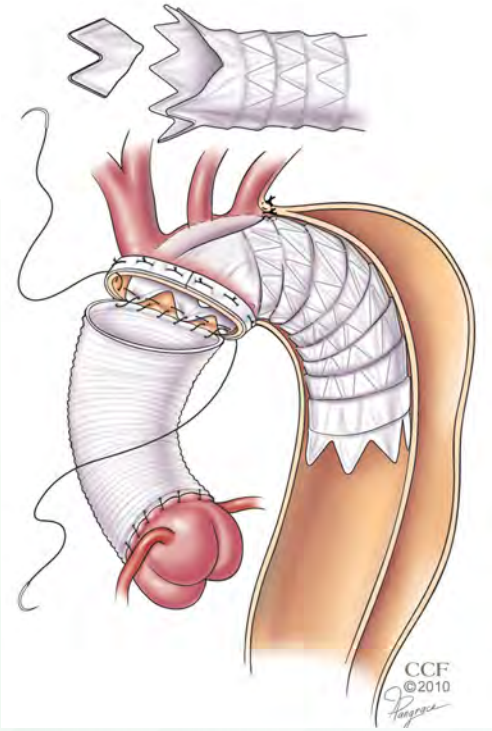
Clinical Failure:
H0: Pt ≥ 0.35 vs. H1: Pt < 0.35
Results:
13.0% (7/54), p-value <0.001
95% CI: 5.37, 24.90

1. **References for PG**: Bashir et al. *Aorta* 2014; Brat et al. *JCTS,* 2015; Chakos et al. *Ann Cardiothorac Surg* 2018; DeRango et al. *J Vasc Surg 2015;* Hiraoka et al. *JTCVS*, 2017; Iba et al. *JTCVS* 2013; Joo et al. *JTCVS* 2018; Thomas et al. *JTCVS*, 2012
2. Line for TRIOMPHE Expected rate is included in graph and estimates how Nexus was expected to perform
3. MAE includes: Early Mortality, Disabling Stroke, Permanent Paralysis/Paraplegia, Renal Failure (Permanent Dialysis), Aortic Rupture

January 2016:
Dr. Eric Roselli & Branched FET (Phaster)

ARTIVION

Circa 2009



Circa 2011

Circa 2015

Circa 2018

Circa 2022

20 YEARS OF INNOVATION IN FET SURGERY!

ARTIVION

E-VITA™
OPEN

2005

World's First CE-Marked FET Device

E-VITA™
OPEN PLUS

2008

FEOR STUDY 2019 - 2021
Study Complete
(N=161)

2019

E-VITA™
OPEN NEO

2020

NEOS EUROPEAN REGISTRY
2020 First Enrollment
2023 Enrollment Complete
(N=161)

NEOS APAC REGISTRY
2021 First Enrollment
2024 Enrollment Complete
(N=112)

2021

NEO EDE™

2025

ARTIZEN
Study Commencement

ARCEVO™ LSA
~ APPROVAL

2028

Memphis Cadaver Lab August 13-14, 2021

ARTIVION™

Memphis Cadaver Lab August 13-14, 2021

ARTIVION

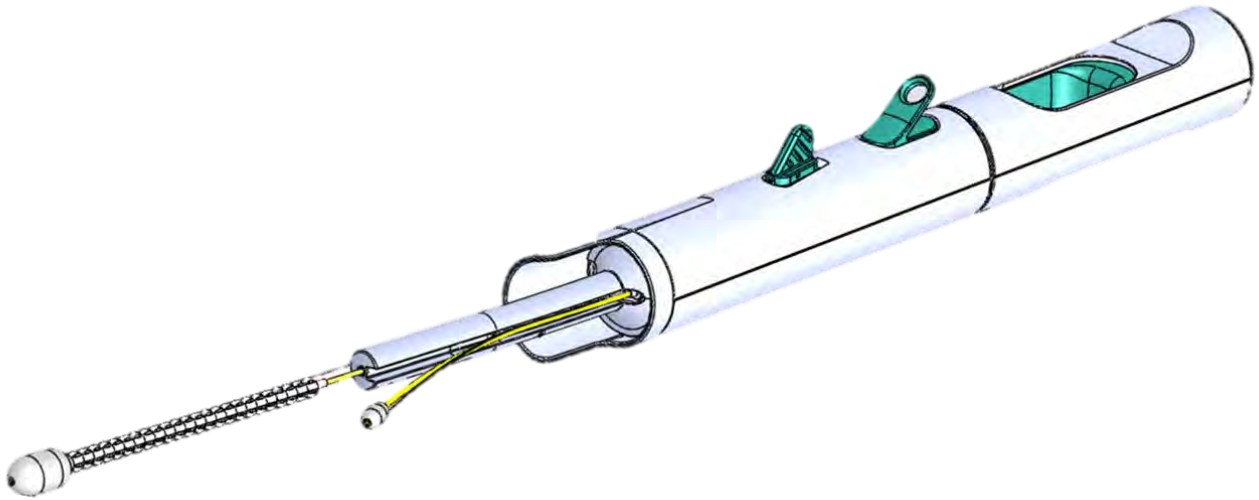
Frankfurt Lab March 12, 2022

Frankfurt Lab March 12, 2022

ARTIVION

Arcevo™ LSA

Hybrid Stent Graft System



ARTIZEN PIVOTAL IDE STUDY

ARTIVION

Prospective, Non-randomized, Non-blinded, Double-arm, Multicenter (US & EU ≈ 30 Sites)

PRIMARY PATIENT GROUP

117 patients: Chronic dissection or Aneurysm

Primary endpoint: Freedom from major adverse events (MAEs) within 1-year post-index procedure: all-cause mortality, new permanent disabling stroke, new permanent paraplegia and/or paraparesis, unanticipated aortic reoperation in the treated segment, LSA occlusion

SECONDARY PATIENT GROUP

15 patients: Acute or subacute dissection

Descriptive statistics: No pre-defined endpoint

REFERENCE COHORT

Historical controls freedom from MAE rate of 59%.

Positive outcome is freedom from MAE composite ≥74%

STUDY STATUS

1ST Enrollment	~ Oct 2025
Enrollment	~ 2025-2026
Follow Up	~ 2027
Approval	~ 2028

R&D PIPELINE

ARTIVION

	Regulatory Path	2025	2026	2027	2028	2029
Hybrid Dissection Prosthesis AMDS 	US PMA					
	Japan					
Endovascular Arch Branch System NEXUS 	US PMA					
	Japan					
Hybrid Frozen Elephant Trunk Arcevo LSA 	US PMA					
	Japan					
Endovascular TAAA System Extra-Design 	US PMA					
	EU					> 2028

Meeting Objectives & Team Introductions

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Purpose

Purpose of the 1st Investigator Meeting

- In-depth protocol and device training with a multidisciplinary, global, group of people from the Sponsor
  - Goal is to ensure understanding and therefore future compliance
  - Training during SIVs is more abbreviated due to time limitations
- Communicate expectations and share high-level study details
- Engage and collaborate with other site investigators and study teams
- Get to know the Artivion Team:
  - Site monitors
  - Site project managers
  - Therapy Manager (for device training/case support)
  - Non-clinical team (i.e., Regulatory, Marketing, R&D, Quality)
  - Leadership team
- Troubleshoot potential issues
- Gather site feedback- so please ask questions (in-person or through the virtual meeting)

Team Members

Clinical Study Team (US Sites)

Team E-mail:
ARTIZEN@artivion.com

Marshall Stanton, M.D.
Sr. Vice President,
Clinical Research and
Chief Medical Officer

Erin Adams
Sr. Director, Aortic Arch
Technologies
Erin.adams@artivion.com

Stephanie Beall
Principal Clinical Research
Project Manager
Stephanie.beall@artivion.com

Casey Jacketta
Principal Clinical Research
Project Manager
Casey.Jacketta@artivion.com

Alecia Charles
Clinical Research Project Manager
Alecia.charles@artivion.com

Sarah Weber
Clinical Project Specialist
Sarah.weber@artivion.com

Monitoring Team

Itohan (Itee) Idugie
Lead CRA, Clinical Operations
Itohan.Idugie@artivion.com

Neoka Wofford
CRA II
Neoka.Wofford@artivion.com

Nibo Umaigba
CRA II
Nibo.Umaigba@artivion.com

Cecilia Nanakumo
CRA II
Cecilia.nanakumo@artivion.com

Daniel Awoniyi
CRA II
Daniel.awoniyi@artivion.com

US Case Support and Training Team

Don Jolley
Sr. Manager, Therapy Development
Don.jolley@artivion.com

Katie Cameron
Sr. Manager, Therapy Development
Katie.cameron!@artivion.com

Sites and Study Partners

Site List:

Site Name	City	State/ Country	Site PI
Allegheny	Pittsburgh	PA	Michael Halbreiner
Baylor Scott & White The Heart Hospital Plano	Plano	TX	William Brinkman
Cleveland Clinic	Cleveland	OH	Patrick Vargo
Columbia University Medical Center	New York	NY	Hiroo Takayama
Cornell	New York	NY	Christopher Lau
Emory University School of Medicine	Atlanta	GA	Brad Leshnower
Jefferson	Philadelphia	PA	Joe Bavaria
Johns Hopkins	Baltimore	MD	Mehrdad Ghoreishi
Medstar	Northwest	DC	Christian Shults
Montefiore	New York City	NY	Joseph DeRose
Northwell Health	New York	NY	Derek Brinster
Northwestern University	Chicago	IL	S. Christopher Malaisrie
University of Alabama at Birmingham	Birmingham	AL	Kyle Eudailey
University of Colorado Hospital	Aurora	CO	T. Brett Reece
University of Florida/Shands	Gainesville	FL	Eric Jeng
University of Michigan	Ann Arbor	MI	Shinichi Fukuhara
University of Pennsylvania	Philadelphia	PA	Nimesh Desai
University of Pittsburgh Medical Center	Pittsburgh	PA	Ibrahim Sultan
University of Southern California	Los Angeles	CA	Fernando Fleischman
University of TX-Austin	Austin	TX	George Arnaoutakis
University of Texas, McGovern Medical Center	Houston	TX	Anthony Estrera
University of Washington	Seattle	WA	Chris Burke
Wisconsin Medical Center	Madison	WI	Jorge Mascaro
German Heart Center at Charite Berlin	**Berlin**	**Germany**	**Joerg Kempfert**
Leipzig Heart Center	**Leipzig**	**Germany**	**Michael Borger**
Universitätsklinikum Freiburg	**Freiburg**	**Germany**	**Martin Czerny**
Hietzing Hospital	**Vienna**	**Austria**	**Martin Grabenwöger**
St. Bart's	**London**	**UK**	**Aung Oo**
University of Bologna	**Bologna**	**Italy**	**Davide Pacini**

23 US Sites

6 EU Sites

Monitor Site Assignments

Neoka Wofford	Nibo Umaigba	Cecilia Nanakumo	Daniel Awoniyi
Medical College of Wisconsin	Columbia	Allegheny	Baylor Scott & White
Medstar Washington Hospital	Emory	Cleveland Clinic	Northwell
Northwestern	Montefiore	Jefferson Health	University of Alabama/Birmingham
University of Colorado	University of Florida	Johns Hopkins	University of Texas, McGovern
University of Michigan	University of Pittsburgh	Cornell	University of Texas, Austin
University of Southern California		University of Pennsylvania	University of Washington

Clinical Research Organization (CRO)

CRO Information:

- **Name**: Bright Research
- **Address**: 730 Second Avenue South, Suite 500, Minneapolis, MN 55402
- **General Email**: info@brightresearch.com

Responsibilities:

- iMedNet EDC build and maintenance
- DSMB & CEC Management
- Safety Management

Contact Information (Safety):

- **Contact Name**: Michelle Doyle
- **E-mail**: Michelle.doyle@brightresearch.com
- **Phone Number**: 720-201-0530

Imaging Core Laboratory

Core Lab Information:

- **Name**: Cleveland Clinic, Vascular Core Laboratory
- **Address**: 9500 Euclid Ave. JJ65, Cleveland, OH 44195
- **General E-mail**: corelab@ccf.org
- **Imaging Upload System**: AGMedNet (Phone Number: 1-888-924-6336, E-mail: support@agmednet.com)

Responsibilities:

- Train sites on diagnostic imaging recommendations and use of program for uploading imaging files
- Provide a detailed qualitative and quantitative diagnostic image analysis for all required imaging
- Identify and/or investigate all instances of suspected device integrity issues
- Communicate and document Significant Findings
- Serve as subject matter expert, as needed
- Support abstracts, presentations, and publications, as needed

Contact Information:

- **Name**: Paul Bishop, Ph.D. RVT, Director - Vascular Core Lab
  - **E-mail:** bishopp@ccf.org
- **Name**: Sara McDaniel, Imaging Specialist I
  - **E-mail**: riskos@ccf.org

Central Institutional Review Board (IRB)

Central IRB Information:

- **Name**: WIRB Copernicus Group
- **Address**: 5000 Centregreen Way, Suite 200, Cary, NC 27513
- **General E-mail**: clientservices@wcgirb.com
- **General Phone**: 855-818-2289
- **System:** Connexus

Responsibilities:

- Reviewing research proposals
- Protecting participant rights and welfares
- Monitoring ongoing research
- Approving, modifying, or disapproving research
- Reviewing changes to research and continuing review
- Addressing safety issues

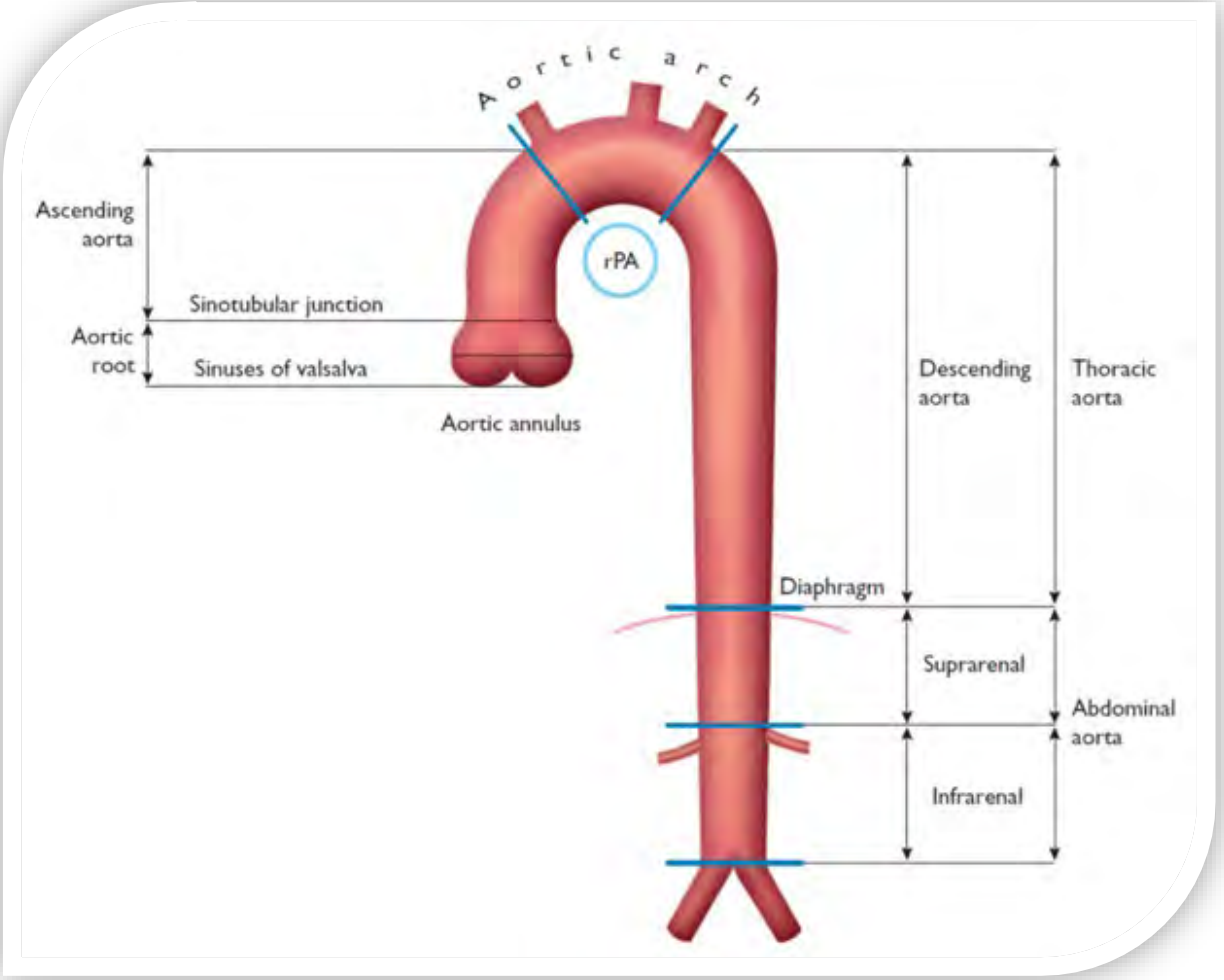
Clinical Background

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Disease State

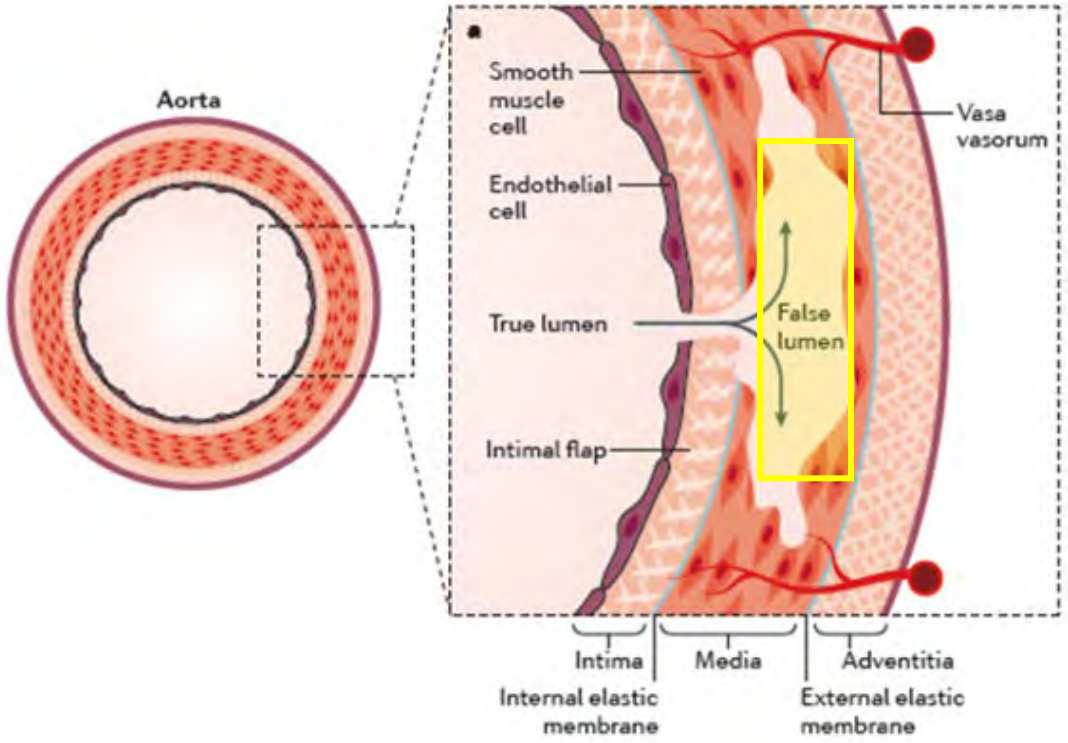
Target Anatomy Overview

- The aorta is the largest blood vessel in the body which delivers blood to vital organs throughout the head and body.
  - o Figure illustrates the aortic segments
- The aortic wall is made up of 3 layers:
  - o Inner layer (intima)
  - o Middle layer (media)
  - o Outer layer (adventitia)
- These 3 layers are impacted differently, depending on the type of aortic disease.



Aortic Dissection Overview

- Dissections develop when there is a tear in the intimal or medial layers of the aorta, which results in separation of the aortic wall (entry tear).
- The dissection results in the aorta having a true lumen (TL) and a false lumen (FL)
  - o TL: native path the blood takes when there is no dissection
  - o FL: new path the blood takes between the layers of the aorta (see figure)
- FL flow can cause:
  - o Aortic insufficiency
  - o Malperfusion
  - o Obstruction of the branch vessels
  - o Aneurysm that could cause a rupture



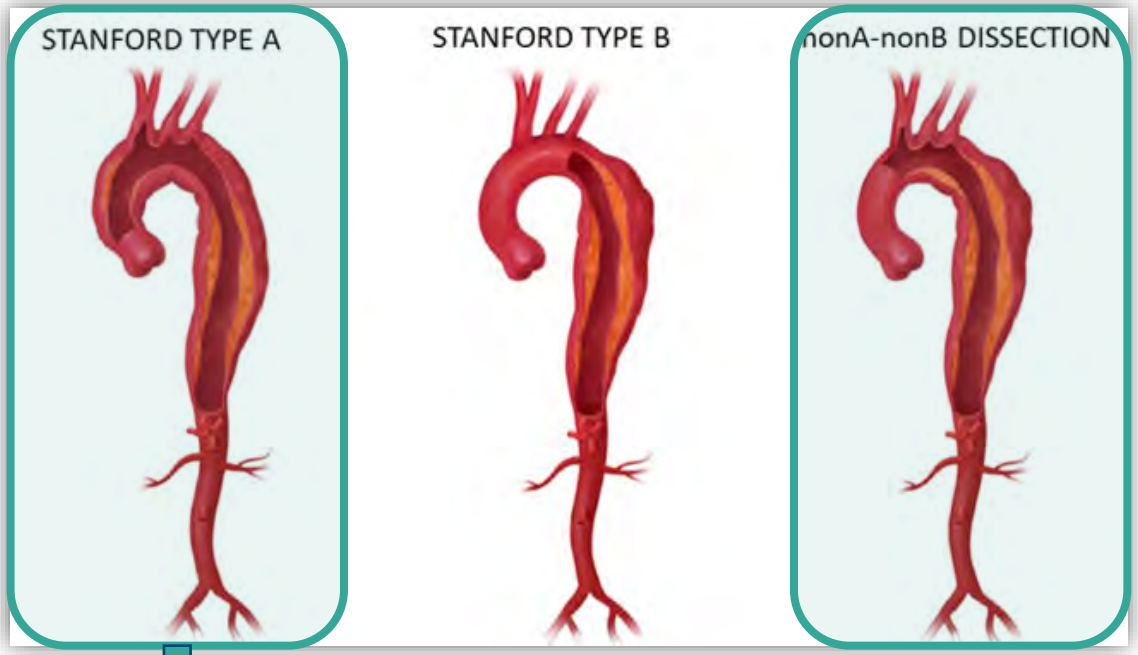
Aortic Dissection Overview, cont.

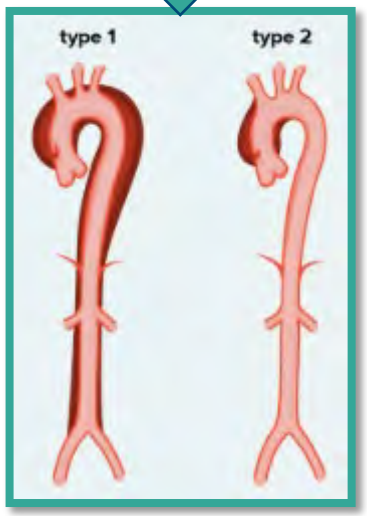
- Classified based on the entry tear location and which aortic segments are involved.
- The (modified) Stanford Classification system specifies disease affecting at least the following segments:
  - Type A: ascending, arch, and descending*
  - Type B: descending
  - nonA-nonB: arch and descending*

Note: the disease of interest for this study affects the arch, at a minimum

- Also categorized by timing of disease onset:
  - Acute: 0-14 days
  - Subacute: 15-90 days
  - Chronic: ≥91 days

Note: acute and subacute will be included in the secondary arm and chronic the primary arm





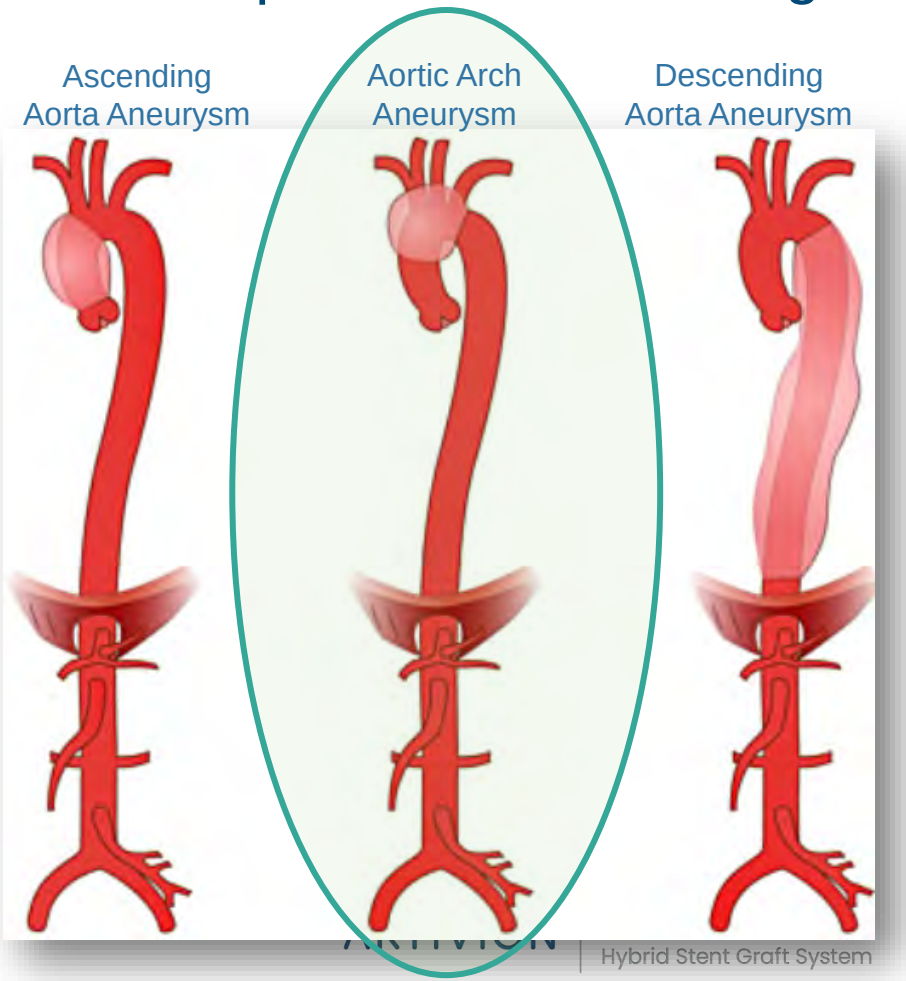
Debakey Classification

- Type 1: Ascending, arch, and descending
- Type 2: Ascending only

Aortic Aneurysm Overview

- A dilation impacting ***all*** layers of the aorta, which is 50% more than the normal expected vessel diameter.
- The expected arterial diameter would be dependent on multiple factors including:
  - o Aortic segment
  - o Age
  - o Sex
  - o Blood pressure
- Aneurysms can affect the following segments individually or in combination:
  - o Ascending aorta
  - o Aortic arch*
  - o Extend distally into the descending aorta

Note: the disease of interest for this study affects the arch, at a minimum



Incidence and Clinical Sequelae

Dissection

- 6,000-10,000 cases annually in the US (Hiratzka LF, 2010)
- 60% of acute dissections have the intimal tear in the ascending aorta and 23% are in the aortic arch (Lansman SL, 1999)
- Acute dissection has a high mortality rate without emergency surgical intervention
- Most patients with chronic dissection are those who had a prior unsuccessful ascending aorta surgery to treat Type A acute dissection

Thoracic Aortic Aneurysm

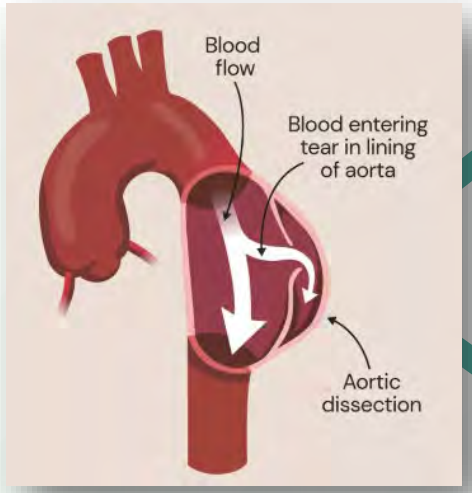
- 26,000 cases annually estimated as a pooled incidence by a recent meta-analysis (Gouveis R, 2021), with a North American rate of 36,500 cases annually (including rupture)
- Often involves multiple segments of the aorta

1. Which area of the aorta must be indicated, at a minimum, to be eligible?

Standard of Care

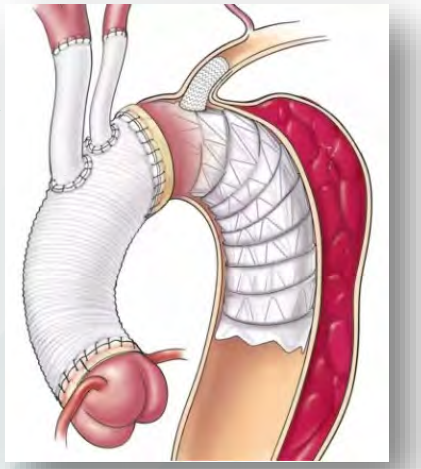
Standard of Care & Alternative Treatment

Acute Aortic Dissection

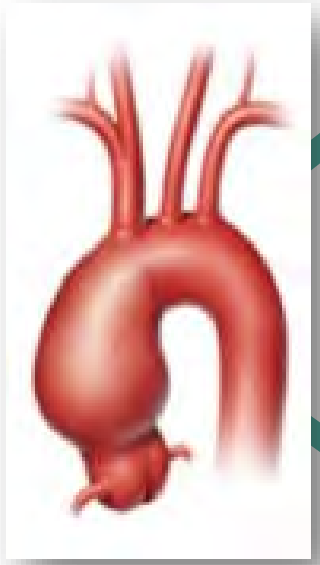


Hemiarch + AMDS

Frozen Elephant Trunk (FET)

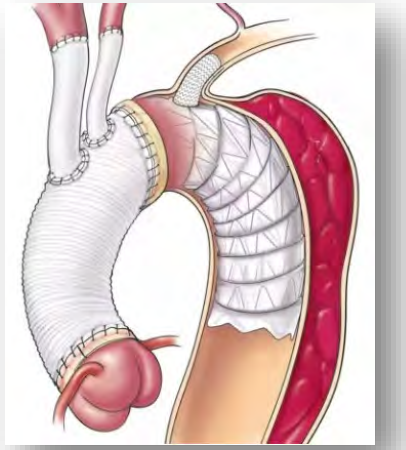


Aortic Aneurysm or Chronic Dissection



Nexus Aortic Arch Stent Graft

Frozen Elephant Trunk (FET)



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

20 YEARS OF INNOVATION IN FET SURGERY!

ARTIVION

E-VITA™
OPEN

2005

World's First CE-Marked FET Device

E-VITA™
OPEN PLUS

2008

FEOR STUDY 2019 - 2021
Study Complete
(N=161)

2019

E-VITA™
OPEN NEO

2020

NEOS EUROPEAN REGISTRY
2020 First Enrollment
2023 Enrollment Complete
(N=161)

NEOS APAC REGISTRY
2021 First Enrollment
2024 Enrollment Complete
(N=112)

2021

NEO EDE™

2025

ARTIZEN
Study Commencement

ARCEVO™ LSA
~ APPROVAL

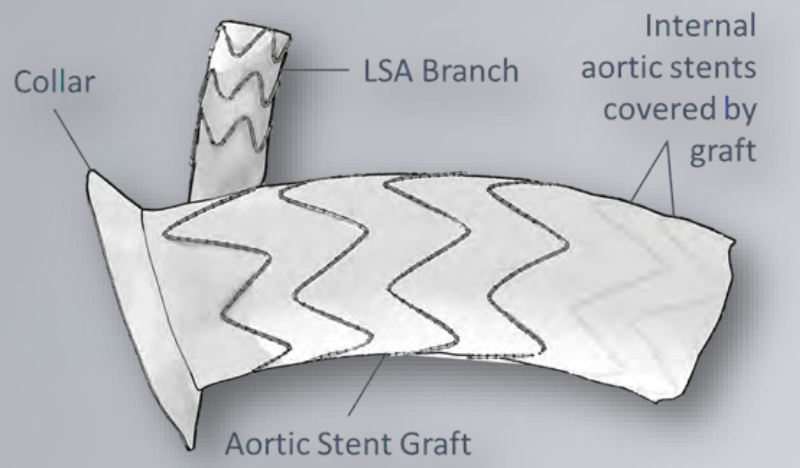
2029

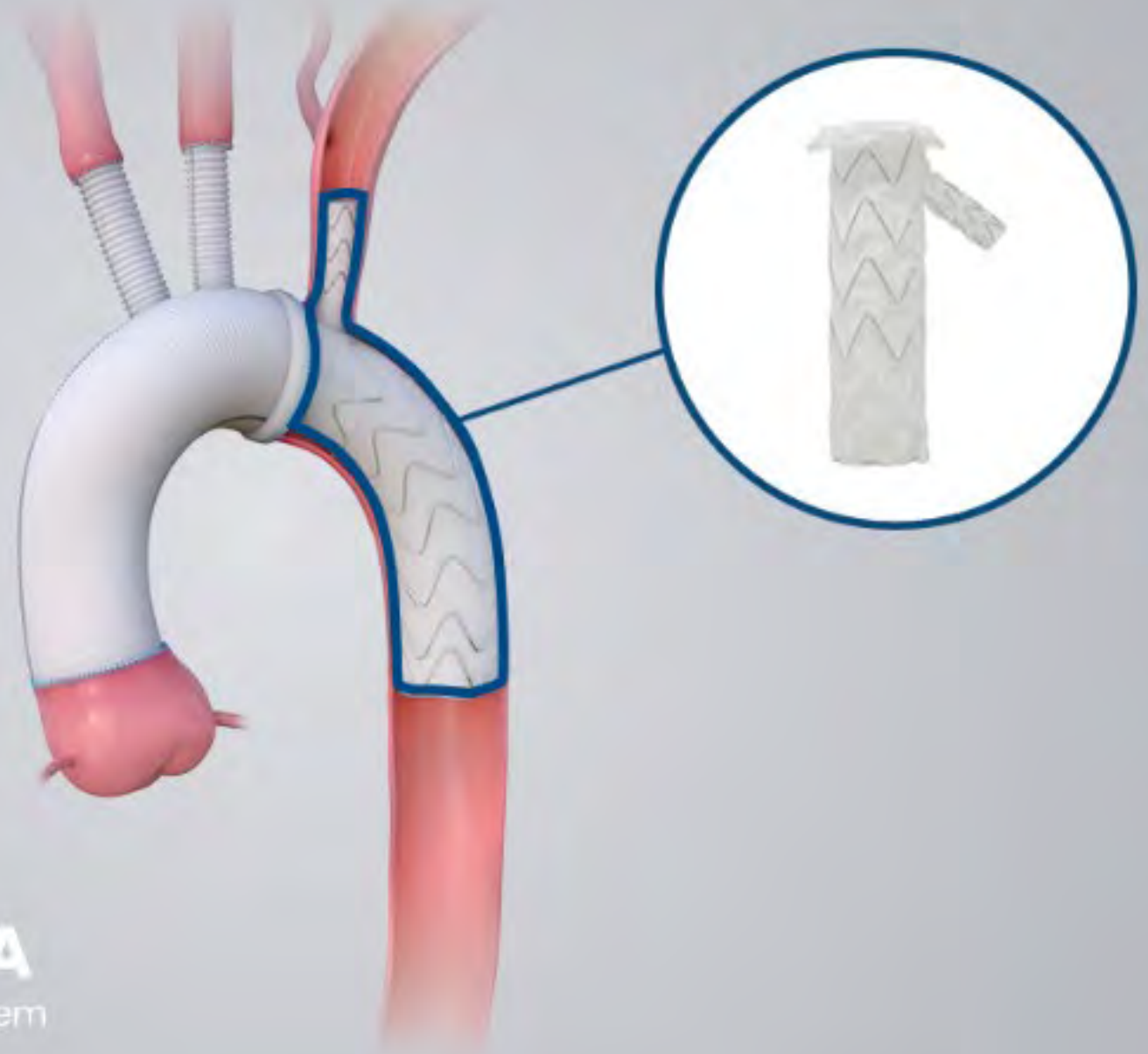
Unmet Need

Unmet Need

- In patients with comprehensive aortic arch disease, a TAR procedure is often indicated – with or without a FET.
- FET repair has several benefits including stent support of the true lumen in dissections, positive aortic remodeling, and resolving malperfusion[3]
- However, FET repair also has the following challenges:
  - Requires management of supra-aortic vessels
  - Adequate cerebral perfusion needed to prevent stroke or other neurological deficits
  - Longer surgical duration involving complications related to cardiopulmonary bypass (CPB) (i.e., low cardiac output, respiratory failure, infection)
- The LSA anastomosis in TAR/FET procedures is often challenging due to its position in the chest cavity, fragility, and the risk of nerve injury[2]
- Performing a more proximal TAR/FET repair with anastomosis in zone 2 may reduce circulatory arrest time, bleeding complications, nerve injury, and reduce the risk of mortality[1] [3]

[1]Roselli et al. Branched stented anastomosis frozen elephant trunk repair: Early results from a physician-sponsored investigational device exemption study. JTCVS 2024 September; 168,3:746-756.
[2]Gambardella I and Girardi L. Total arch replacement: Technical pearls. JTCVS Tech. 2021 May 19; 10:8-13.
[3]Goel et al. Malperfusion in Patient with Acute Type A Aortic Dissection: A Nationwide Analysis. Ann Thorac Surg. 2025 Jan; 119:980-9.





ARTIVION | Arcevo™ LSA
Hybrid Stent Graft System

Protocol Overview

ARTIVION™ | **Arcevo™ LSA**
Hybrid Stent Graft System

Study Design

Regulatory Status

- **FDA Approval:** July 16, 2025
- **IDE Number**: G250152
- **Clinicaltrials.gov Number:** NCT07089576
- In the United States and Europe, Arcevo LSA will be an investigational, significant or high risk (Class III) device.
- Medtronic's Valiant™ Captivia™ is approved for all indicated uses in the US and Europe but will be investigational in this study.
- CMS Category B Approval on September 4, 2025
    - o Reimbursement guides will be provided at the end of October

Study Summary

- **Study Title:** A Prospective, Multi-center Clinical Study to Evaluate the Safety and Effectiveness of Arcevo™ LSA in the Open Repair of Aortic Arch Aneurysms and Dissections: ARTIZEN
- **Study Design:** Prospective, non-randomized, non-blinded, double-arm, multi-center interventional study
- **Sites:** Up to 30 sites in the US and EU
- **Enrollment:** 132 enrolled patients and approximately 184 consented patients (28% estimated SF rate)
  - Target minimum per site is 5 patients; site max is 20 patients
  - Anticipated enrollment period: 18-21 months
  - Primary arm (n=117): patients with an aneurysm or chronic aortic dissection
  - Secondary arm (n=15): patients with acute or subacute aortic dissection
- **Follow-up:** Enrolled patients will have 5-years of follow-up visits, with 10 data collection timepoints as follows:
  - Pre-op
  - Procedure
  - Hospital Stay
  - 30-days (dependent on when discharge occurs)
  - 6-months
  - 1 yr, 2 yrs, 3 yrs, 4 yrs, and 5 yrs
- **Study Duration:** 6-7 years depending on time to enrollment completion
- The study will enroll in 2 Phases, at FDA's request:
  - Phase I will include enrollment of up to 30 patients
  - After FDA Approval, Phase II will include enrollment of the remaining 102 patients

Study Objectives

Primary Objective

- Demonstrate a clinically meaningful increase in the number of patients free from the following major adverse events (MAEs) within 1 year of the index procedure (i.e., when Arcevo™ LSA is implanted):
  - All-cause mortality
  - New permanent disabling stroke
  - New permanent paraplegia and/or paraparesis
  - Unanticipated aortic re-operation in the treated segment
  - Left subclavian artery (LSA) occlusion

Secondary Objectives

- Demonstrate acceptable rates of:
  - Long-term mortality
  - Additional aortic procedures
  - Device-related events
  - Other MAEs
  - Radiographic events as determined by the imaging Core Lab
  - Dissection-related events
  - Thoracic extension (i.e.,TEVAR) related events
  - Technical, procedure, and treatment-related success

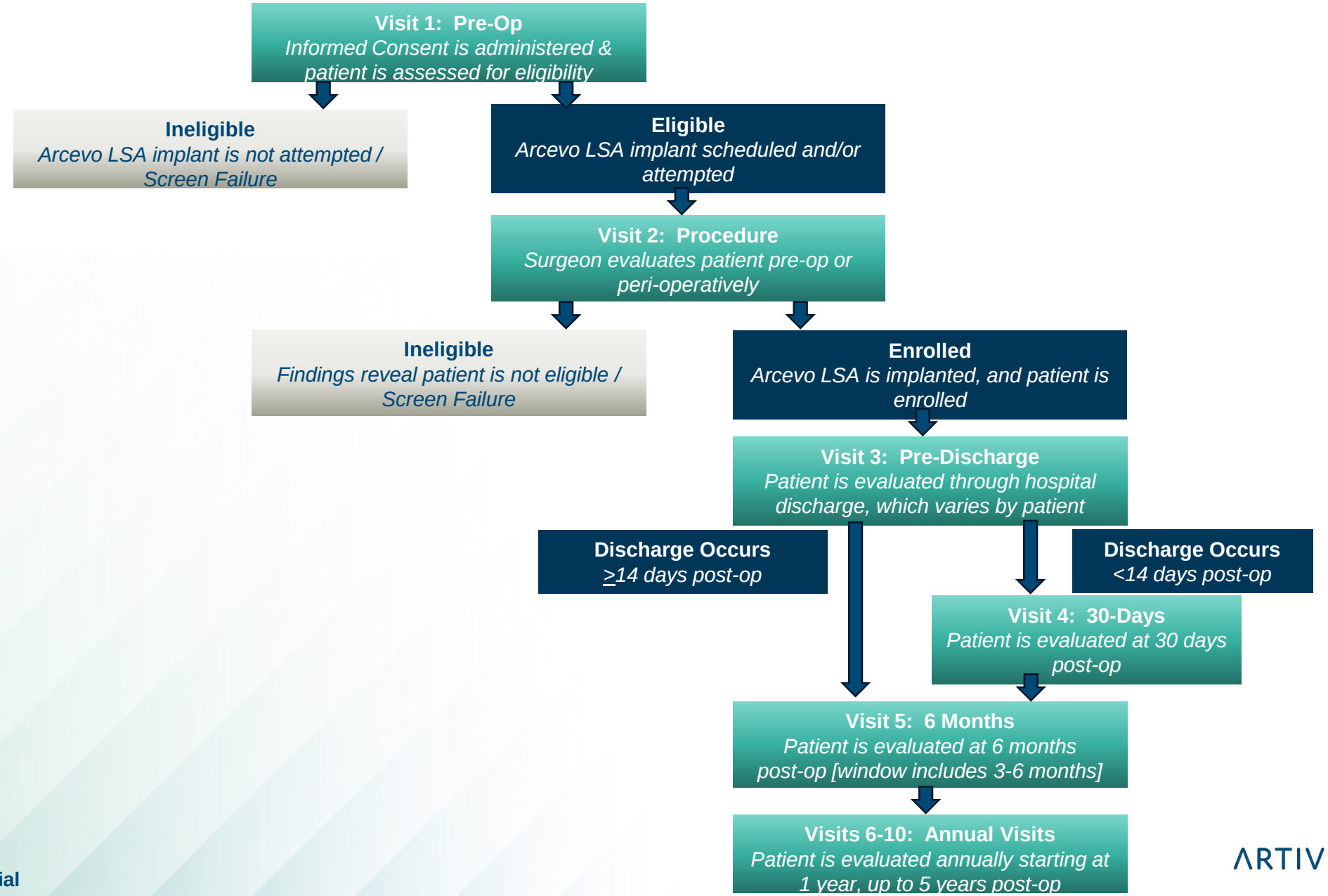
Exploratory Objectives

- Analyses planned to evaluate quality of life using the 12-Item Short-Form Survey (SF-12v2)

2. Wht type of patients are enrolled into the primary arm?

Schedule of Activities

Study Flow Chart



3. At what time point is the patient considered enrolled into the study?

Schedule of Assessments

Protocol Required

Data Collected only if performed as SoC

PROTOCOL ACTIVITY	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visits 6-10
	Pre-Procedure	Procedure (within 90 days of consent)	Hospital Stay	30-days	6 months	1, 2, 3, 4, 5 years
		<24 hrs post-op	*≥ 24 hrs post-op through discharge*	*+/-14 days*	*+ 4 / -14 weeks*	*1yr: +/- 8 weeks 2-5 years: +/-12 weeks*
Informed Consent, Eligibility, Demographics, Pregnancy Test, & Baseline Assessments	X					
Concomitant Medications	X		X	X	X	X
Blood Tests	X		SoC	SoC	SoC	SoC
Physical Exam	X		X	X	X	X
CTA Imaging	X	SoC	X *(within 7-44 days post-procedure)*		X	X
Brain Imaging	X (patients w/hx of stroke in Primary Arm)	SoC	SoC	SoC	SoC	SoC
Modified Rankin Scale	X	*If Stroke Occurs*	*If Stroke Occurs*	*If Stroke Occurs*	*If Stroke Occurs*	X (at 1 yr if stroke occurred) *If Stroke Occurs 2-5 yrs*
Modified Tarlov Scale	X		X	X	X	X
SF-12v2 QOL	X (Primary Arm only)		X	X	X	X
NIHSS		*If Stroke Occurs*	*If Stroke Occurs*	*If Stroke Occurs*	*If Stroke Occurs*	*If Stroke Occurs*
Treatment Planning & Device Sizing	X					
Procedure & Device Technical Success Assessment		X				
Adverse Event Assessment		X	X	X	X	X
Hospital Stay Assessment			X			
Additional Post-operative Procedures			X	X	X	X
Study Exit			X (can occur at any point)			

4. At what study visit(s) is brain imaging required?

Lab Assessments: Blood Tests

Protocol Required | Data Collected only if performed as SoC

- Blood test data will not be reviewed by an independent Core Lab.
- At a minimum, the blood test data will be used to support AE evaluations.

Blood Test	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visits 6-10	SAE w/ Hospitalization[1]
	Pre-Op	**Procedure** <24 hours post-op	**Hospital Stay** ≥ 24 hrs post-op through discharge	**30-day Follow-up**	**6-month Follow-up**	**Years 1, 2, 3, 4, and 5**	***As applicable***
βhCG Pregnancy Test[2]	X						
Creatinine	X		SOC	SOC	SOC	SOC	SOC
Blood Urea Nitrogen (BUN)	SOC		SOC	SOC	SOC	SOC	SOC
High Sensitivity Troponin	SOC		SOC	SOC	SOC	SOC	SOC
International Normalized Ratio (INR)	SOC		SOC	SOC	SOC	SOC	SOC
Platelets	SOC		SOC	SOC	SOC	SOC	SOC

βhCG = Beta-human chorionic gonadotropin; Pre-op = preoperative; SOC=Standard of Care; SAE: Serious Adverse Event

1 All applicable blood tests will be collected as part of SAE reporting and evaluation (including those not included in this table)

2 Applicable only to individuals of childbearing potential, or individuals for whom childbearing potential is uncertain. This test may be completed using a laboratory assay of blood or urine sample, or by a urine point-of-care test.

Schedule of Assessments: Screening

- Informed consent must be obtained ≤ 90 days of procedure and prior to uploading pre-procedure images to the core lab
- Anatomical eligibility should be assessed with a CTA completed within 90 days of the consent
- Rescreening
  - Patients that screen fail may be rescreened; to rescreen a patient, site must obtain sponsor approval
  - If rescreening is approved, CTA may need to be repeated if rescreening occurs >90 days from date of CTA
- After obtaining informed consent, a new patient should be created in the EDC
  - eCRFs required for all consented patients:
    - Registration
    - Eligibility assessment
    - Demographics
    - Pregnancy evaluation (if applicable)
- Assessments included in Visit 1 (eCRF entry can occur after enrollment):
  - Medical, cardiac and social history
  - Baseline/pre-op imaging evaluation and upload to core lab portal
  - mRS
  - Modified Tarlov Scale
  - Malperfusion at presentation (secondary arm pts. only)
  - Concomitant Medication (antiplatelets, anticoagulants, blood pressure medication *only*)
  - Physical exam (BP, other vital if collected SOC)
  - Blood test (creatinine, pregnancy test if urine test not administered and as appliable)
  - SF-12 (primary arm patients only)

5. If a patient is a screen failure, they cannot be rescreened.

Schedule of Assessments: Enrollment

- A patient is enrolled after implantation of the Arcevo LSA device
- After a patient is enrolled, the following Visit 2 eCRFs are required within 3 business days:
  - Treatment planning & device sizing
  - Procedure
    - Completion of the procedure CRF will notify site PM and CRA of enrollment
    - This allows Artivion to track overall enrollment progress, especially given phases
      - Starts “timer” for date of monitoring visit (if first enrollment)
    - Triggers re-stock of the device used in the procedure (if part of starter-pack)
    - If there is an anticipated delay in Procedure eCRF data entry, please notify the study team at ARTIZEN@artivion.com of device implant.
  - Device technical success
  - Adverse event assessment
  - Brain imaging (if post-op stroke ***and*** collected as SOC)
  - mRS (if post-op stroke)
  - NIHSS (if post-op stroke)

Schedule of Assessments: Hospital Discharge / 30-Day Visit

- Data between the procedure and hospital discharge will be collected on the Hospital Stay Assessment eCRF
  - If a patient dies prior to hospital discharge, a Hospital Stay Assessment is still required, as well as a Study Exit form
- 30-day visit will occur only if patient was discharged from the hospital less than 14 days from Arcevo LSA device implantation
- If the patient is discharged from the hospital more than 14 days from Arcevo LSA implantation, data will be collected for the 30-day visit, with a focus on new information or events occurring between discharge and the 30-day window
  - 1 CTA scan is required between 7- and 44-days post-procedure, which could occur during hospitalization or during the 30-day visit window.
    - Even if the visits are distinct, only 1 CTA is needed
  - Coordinator could also capture any new vital assessments, blood tests, con-meds, or adverse events
  - SF-12 should be completed before discharge and at the 30-day visit, unless the windows overlap
    - If necessary, SF-12 surveys could be completed over the phone

Schedule of Assessments: Stroke

- **Diagnostic Brain Imaging**:
  - For patients in the primary arm with hx of stroke, pre-op brain imaging (CTA or MRI) is required ≤ 90 days prior to the procedure
    - This pre-procedure information is important to be able to assess post-procedure changes in the event of stroke
    - The Brain imaging file may be requested for evaluation by the CEC or Core Lab, but standard upload of the imaging file is not planned
  - For patients who experience a post-op neurological event, brain imaging information will be collected in our eCRFs, if imaging was done per the site's SOC; it is not required per the protocol
  - Information from the site's brain imaging report will be entered into the Brain Imaging eCRF
- **Modified Rankin Scale (mRS)**:
  - Required pre-op for both study arms
    - For patients in the secondary arm, mRS can be finalized post-op based on information collected before surgery
  - Required post-op only if stroke occurs in either study arm throughout follow-up
  - mRS should be completed within a reasonable amount of time after the event occurs (i.e., <1 week)
  - Can be completed by any site member who is delegated the task on the DOA and has completed certification
  - For any patient with a stroke <1 year from Arcevo LSA implantation, an updated mRS assessment is required at 1-year
  - Information will be entered into the mRS eCRF
- **NIHSS**:
  - Required if a patient experiences a post-op stroke
  - NIHSS should be completed within a reasonable amount of time after the event occurs (i.e., <1 week)
  - Can be completed by any site member who is delegated the task on the DOA and has completed certification
    - If NIHSS is completed by a neurologist as part of a SOC post-stroke evaluation, no additional NIHSS is required
  - Information will be entered into the NIHSS eCRF

Schedule of Assessments: New Paraplegia/Paraparesis

- **Modified Tarlov Scale:**
  - Required for all patients (in both arms) at all visits, expect Visit 2 (Procedure)
  - Information should be entered into the Modified Tarlov Scale eCRF around the time of each visit
  - Can be completed by any site member who is delegated the task on the DOA and has completed certification
- **Note**: Issues with movement may be related to a different issue (ex. stroke), so incidence of paraplegia and paraparesis will be based on site reporting of the event as an AE and the modified Tarlov Scale score will just be used to qualify the event
  - A score <5 will not be considered paraplegia or paraparesis unless the AE is reported by the site

Modified Tarlov Score	
Paraplegia	
0	No lower extremity movement
1	Lower extremity motion without gravity
2	Lower extremity motion against gravity
Paraparesis	
3	Able to stand with assistance
4	Able to walk with assistance
Normal	
5	Normal

Schedule of Assessments: Assessing Vitals and Diagnostic Imaging

- **Physical exam**:
  - Required information includes date of visit, type of visit (in-person or telehealth), reason if visit was missed and blood pressure
  - Additional vital sign assessment (i.e., pulse rate, body temperature) will be collected if performed based on site SOC; no deviations will be issued for missing these vitals

- **Imaging evaluation**:
  - Computed tomography angiography (CTA) is preferred; alternative options can be used if required
  - Imaging of chest, abdomen, and (preferably) pelvis will be collected pre-op and at all follow-up visits
    - Imaging details will be presented by Paul, director of the CCF Imaging Core Lab in later session
  - Sites will enter the visit information (date & type of imaging/ confirm upload) in the Imaging eCRF and the Core Lab staff will complete the remainder of the Imaging eCRFs

Study Procedures: Other

Unscheduled visits:

- If an enrolled patient completes an unscheduled visit, new and significant information will be entered into pre-specified forms in the EDC (ex. AEs, additional procedures)
- If medical imaging is done, it should only be uploaded into the Core Lab database if it aligns with a visit window and there is no imaging already available, or there is an associated AE or device deficiency suspected

Device explant:

- If partial or complete explant of Arcevo LSA or Valiant™ Captivia™ device, data entry into the Additional Post-op Procedure eCRF will be required.
- Any explanted material including Arcevo LSA should be sent to Artivion following the instructions provided in the Investigational Product Inventory Management, which will be provided by your Artivion PM.
- Any explanted material including only Valiant™ Captivia™ may be requested by Medtronic, with specific instructions provided.

Endpoints

Primary Endpoint

- The primary endpoint is a composite for both safety and effectiveness and is defined as the ***freedom from*** rate of the following 5 major adverse events (MAEs) within **≤1 year** of the index procedure (i.e., Arcevo LSA implantation):
  - All-cause mortality
  - New permanent disabling stroke
  - New permanent paraplegia and/or paraparesis
  - Unanticipated aortic reoperation in the treated segment
  - LSA occlusion

- All MAEs (except LSA occlusion) will be assessed based on site reporting and LSA occlusion will be based on Core Lab evaluation
- The sample size for the primary arm (n=117) is based on primary endpoint assumptions:
  - The performance goal (59%) is largely based on results from 4 publications in the literature
  - The expected rate (74%) with Arcevo LSA is based on prior generation (E-vita OPEN NEO) study results

Primary Endpoint (cont.)

- The primary endpoint events are defined as follows:
  - **All-cause mortality:** Death due to any reason – known or unknown.
  - **New permanent disabling stroke**: Post-op stroke (<1 yr from Arcevo LSA implant) with a mRS score of ≥2, a change in mRS of ≥1 (compared to pre-op) *and* an mRS score at 1-year that is unchanged or worsens since mRS at time of post-op stroke event.
  - **New permanent paraplegia and/or paraparesis:** Post-op paraplegia or paraparesis with a modified Tarlov Scale score ≤ Grade 4, with a score reduction of at least 1 point (compared to pre-op) and a score at the 1-year visit that is unchanged or worsens.
  - **Unanticipated aortic reoperation in the treated segment**: any additional unplanned percutaneous, endovascular or surgical procedure occurring after the index procedure that is targeted in the aortic pathology that was treated with the Arcevo LSA device (i.e. aortic arch, proximal descending aorta, LSA)
  - **Left subclavian artery occlusion**: functionally occluded (flow is almost zero) or complete loss of blood flow to the LSA for any reason (assessed by Imaging Core Lab)

Primary Endpoint (cont.)

- Primary endpoint results will be prioritized, since the study's success is based on the outcome
- The site is only asked to report the event (i.e., death, stroke, paraplegia or paraparesis or additional procedure in the treated segment)
  - Qualification of the events (ex. new permanent disabling stroke) will be achieved through programming and take into consideration other available data (ex. mRS or modified Tarlov Scale)
- Timely and complete data entry for any of the 4 MAEs or supporting data (into the AE, Additional Post-Operative Procedure, mRS, and modified Tarlov Scale eCRF) is very important
  - Please enter any known information immediately, even if all details are not available
  - These events will also be closely monitored, so please address queries in a reasonable timeframe
- Additionally, primary endpoint events will be adjudicated, and sites should prioritize any follow-up questions or requests that may come from the CEC

6. How many major adverse events (MAEs) comprise the composite primary endpoint?

Secondary Endpoints

Assessed at all follow-up visits

Mortality

- All-cause mortality
  - Cardiovascular-related mortality
  - Aorta-related mortality
  - Procedure-related mortality
  - Device-related mortality

Additional Aortic Procedure

- All unplanned aortic procedures (endovascular, percutaneous, and open)
- Unanticipated aortic reoperations in the treated segment
- Unanticipated device-related reoperations
- Arcevo™ LSA explant

Device-Related Events*

- Device migration
- d-SINE
- Failed stent patency in the main body
- Failed stent patency in the LSA
- Stent-graft integrity issue compromising flow (i.e., stent fracture, narrowing, kink, or twist)

Composite Success:

- Technical Success
- Procedural Success**
- Treatment Success**

*Assessed by Core Lab

**Calculated by programming and site entry is not required

Secondary Endpoints, cont.

Assessed at all follow-up visits

Radiographic Events*

- Anastomotic leak between Arcevo™ LSA and surgical graft (i.e., Type Ia endoleak or distal anastomotic new entry [DANE])
- Type Ic endoleak (i.e., at the end of the LSA stent component)
- LSA occlusion
- New LSA dissection
- Maximal total aortic diameter growth >1 cm in the treated segment (Zones 2-4) compared to baseline
- Maximal total aortic diameter growth >1 cm below distal end of Arcevo™ LSA, compared annually

Dissection-Related Events Only*

- TL reduction compared to baseline >5.0 mm at maximal total aortic diameter (Zones 2-4)
- FL growth compared to baseline >5.0 mm at maximal total aortic diameter (Zones 2-4)
- FL thrombosis in the treated segment (LSA, Zones 2-4)
- FL thrombosis in the untreated segment (Zone 5)

Thoracic Extension Procedure Only

- Incidence of any failure of device-extension integrity (e.g., wear or tear in the fabric or wire breakage) resulting in a compromised seal and blood leakage or movement of the device *
- Incidence of Type IIIa endoleak *
- Incidence of failed patency of the device-extension overlap *
- Incidence of primary MAEs at 30-days post-extension
- Incidence of secondary procedures related to the extension within 30-days post-extension

*Assessed by Core Lab

Secondary Endpoints, cont.

- Secondary endpoint results are also important, since Artivion will include the results in annual reports to FDA
- For endpoints based on site entry, the site is only asked to report the event (i.e., death, stroke, paraplegia or paraparesis, or additional procedure in the treated segment)
- Timely and complete data into these eCRFs are very important:
  - AE, Additional Post-Op Procedure, Technical Success, Treatment Planning & Device Sizing, Modified Tarlov Scale and Modified Rankin Scale (as applicable), General Medical History, Follow-up (dialysis info)
  - These events will also be closely monitored, so please address queries in a reasonable timeframe
- Timely submission of CTAs into the Core Lab system is very important since there are multiple endpoints based on imaging evaluation
- Additionally, secondary endpoint events will be adjudicated, and sites should prioritize any follow-up questions or requests that may come from the CEC

Data Collection

Data Collection, Documentation, and Verification

- Appropriate source documentation must be available at each monitoring visit to document protocol compliance and CRF entries
  - Source documentation is **the first (original)** document(s) and/or location of the documents at the study site where the source data will be captured/documented
- Optional source worksheets will be provided by Artivion and can be used for any information that is not normally collected in the site's electronic medical record (EMR)
- All reports (imaging, laboratory, etc.) must be signed, dated, and addressed by Investigator as appropriate & included in the source documents
  - Any abnormal lab findings must be reviewed by the PI and assessed as Clinically Significant (CS) or Not Clinically Significant (NCS).
- Medical records must contain appropriate documentation to verify diagnosis, etc.
- CRA requires access to study records and source documents
  - This includes data from referring or other treating physician (ex., mRS, NIHSS, modified Tarlov Scale)
  - The PI is responsible for data entered into eCRFs and other EDC/source tools under their supervision. The data should be reviewed and signed-off within the project specified timelines.

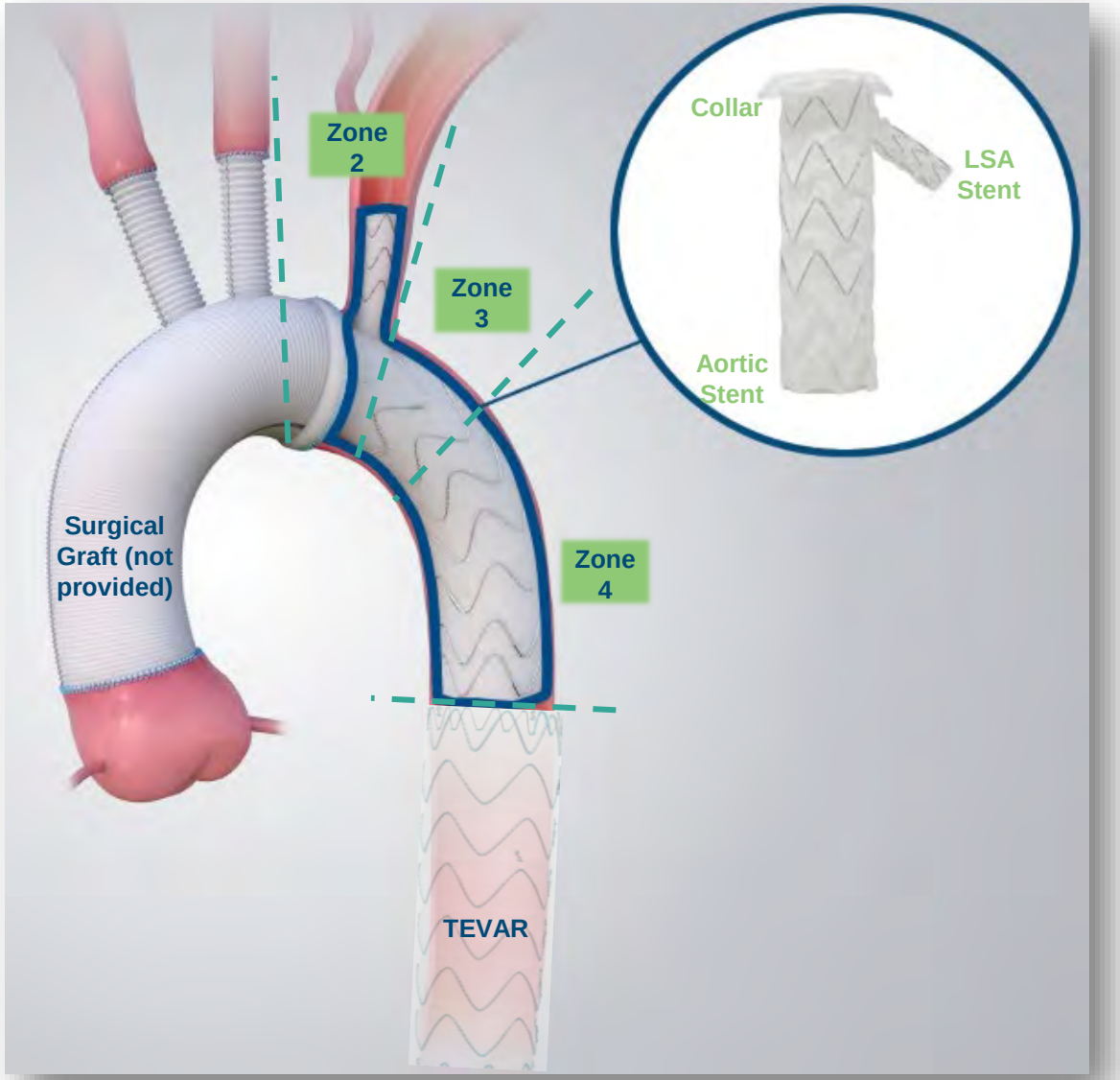
Data Entry Expectations

- Screening and enrollment data is expected to be entered within 3 business days of informed consent and implantation, respectively
  - This includes the following eCRFs: **Registration, Study Eligibility, Demographics,** both **Cardiac** and **General Medical History, Treatment Planning & Device Sizing,** and **Procedure**
- eCRFs will be reviewed for completeness and clarity by CRAs during IMVs and data managers remotely
- eCRFs will also be reviewed by the Bright Safety team for events requiring adjudication
- Queries will be issued within the EDC for any information inadvertently omitted, inconsistent, or not supported by source documents.
  - Data queries should be addressed within 5 business days of query creation
- The site will be responsible for clarification and resolution of all queries
- Queries will be closed after sufficient clarification and resolution is achieved

Potential Benefits and Risks

Arcevo LSA Potential Benefits

- Enables zone 2 open surgical repair of the aortic arch
- Incorporates a stented LSA branch to eliminate the need for the often-challenging LSA anastomosis
- Clear visualization of the aorta and LSA vessel during device insertion & deployment
- Conical shaped collar allows for a robust anastomosis between Arcevo and the chosen surgical graft
- Allows for thoracic endovascular aortic repair (TEVAR), if needed



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Possible Procedure-Related Risks

Possible risks that may be associated with the total arch replacement (TAR) procedure include, but are not limited to (listed in alphabetical order):

- Anemia requiring ≥ 2 units of blood product in a transfusion
- Atrial fibrillation
- Biologic response
- Cardiac failure
- Death
- Fistula
- Hematoma
- Hemorrhage/bleeding
- Hypotension/hypertension
- Infection or fever
- Infectious disease transmission
- Inflammation
- Internal bleeding
- Ischemia-reperfusion injury
- Recurrent laryngeal or phrenic nerve palsy
- Liver failure
- Multi organ dysfunction syndrome or failure
- Gastrointestinal system complications and subsequent problems
- Neurological complications
- Pleural effusion requiring drainage
- Respiratory failure requiring tracheostomy or prolonged ventilation
- Pulmonary complication
- Renal insufficiency and/or renal failure
- Sepsis
- Shock
- Vascular trauma
- Vasoplegic syndrome
- Wound healing complications

Possible Device-Related Risks

Potential risks that may be associated with Arcevo™ LSA device *and/or* TAR procedure include, but are not limited to:

- Allergic reaction to prosthesis material(s)
- Amputation due to upper limb ischemia
- Aortic enlargement (e.g., aneurysm, false lumen)
- Aortic aneurysm rupture
- Dissection/perforation/rupture of the aorta, LSA, and/or vasculature, distal stent induced new entry (dSINE) tears
- Embolism (e.g., thromboembolism, microembolism)
- Endoleak, distal anastomotic new entry tear (DANE) or distal anastomotic leak
- Ischemia or infarction (e.g., cerebral, visceral, renal, organ, peripheral)
- Occlusion (venous or arterial, including prosthesis occlusion)
- Post-implant syndrome
- Prosthesis material failure (including breakage of metal portion of device, collapse, extrusion, erosion, and/or prosthesis rupture)
- Pseudoaneurysm
- Stenosis (arterial or venous including prothesis stenosis)
- Stent graft migration (retrograde in case of aneurysm)
- Stent graft infection
- Thrombosis (including prosthesis thrombosis)

Additional Potential Risks

- Additional device risks can occur due to deviations from the IFU, including:
  - Improper device size selection
  - Delayed device positioning or deployment
  - Device modification
- There may also be unforeseen risks associated with Arcevo LSA or the procedure
- Other risks or inconveniences specific to participation:
  - Radiation risk or exposure to x-rays during diagnostic imaging exams
  - Blood test risk, or some pain and minor discomfort from required blood draws
  - Urine pregnancy test (individuals of child-bearing potential only)

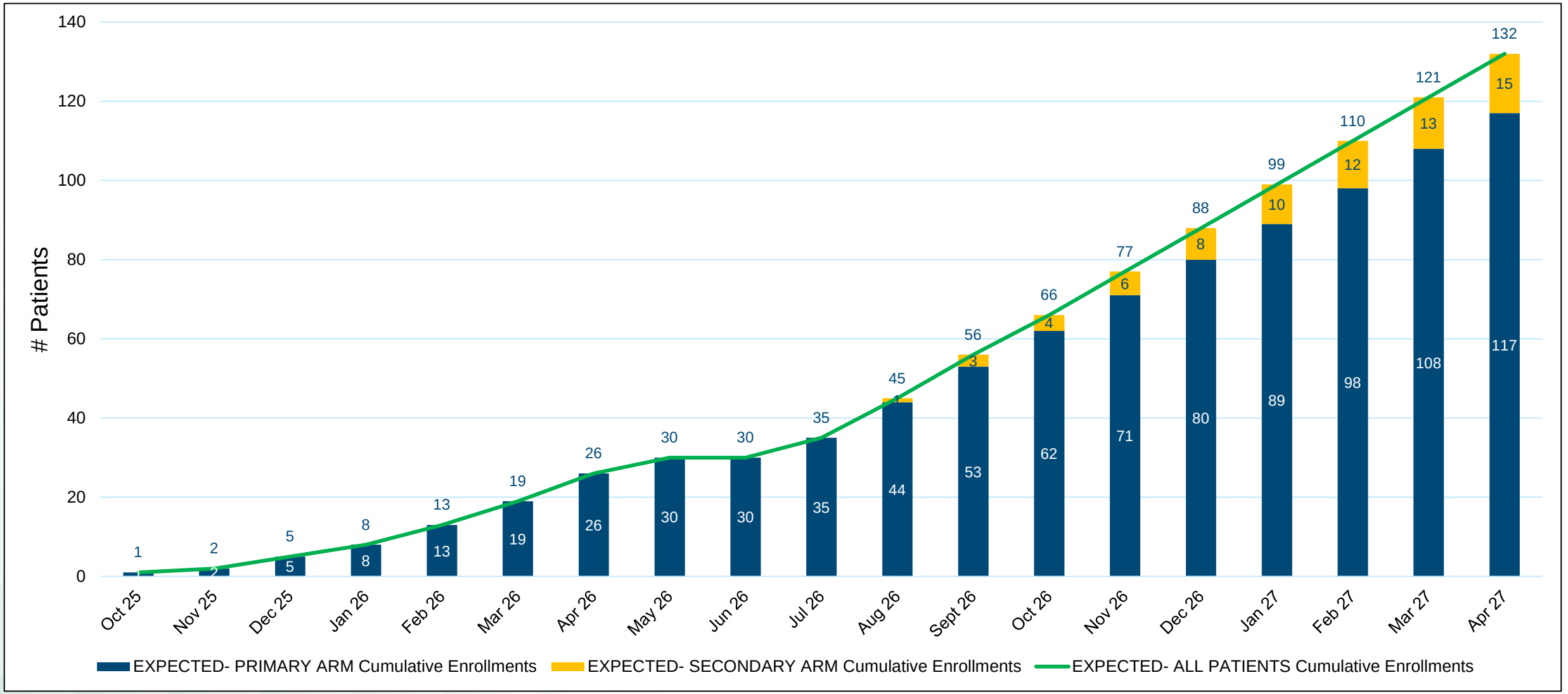
Enrollment Expectations

Site Enrollment Expectations

- Target enrollment for each site is a minimum of **5** patients
- Maximum enrollment per site is **20** patients
- There is no pre-defined expectation on the breakdown of patients within each disease indication
  - However, there is a requirement that the first 2 patients enrolled at each site are in the primary arm (i.e., elective cases), so you will have at least 2 patients who have either chronic dissection and/or aneurysm
- Average estimated enrollment rate per site/per month is 0.4 (or a little less than 1 patient every other month)
- Enrollment is projected to occur over 18-21 months, with Phase I taking 8 months and Phase II taking 10 months (with a pause in between for analysis and FDA review)
- Artivion will be tracking screening activity through pre-screen and screen failure data in the EDC
  - Providing the reason a patient isn't eligible will allow us to ensure your site's understanding of the protocol and/or consider any potential future protocol amendments
- Enrollment activity is tracked by completion of the procedure form in the EDC
- Your Artivion PM may request a meeting to discuss any enrollment challenges

Projected Cumulative Enrollments

Pause in Enrollment in June 2026 – FDA Approval Needed to Move to Phase II



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

7. What are the enrollment minimum and maximum for each site?

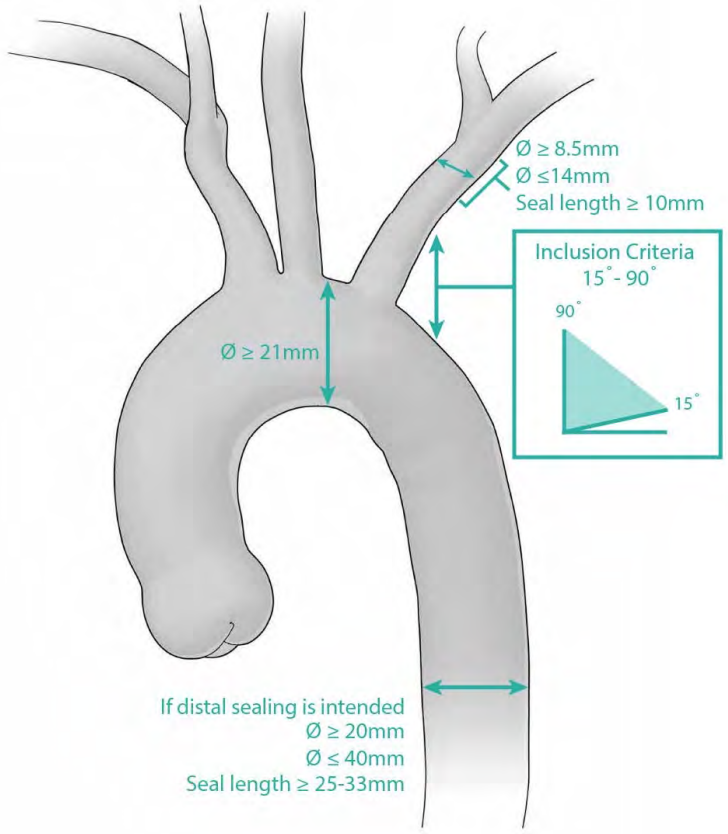
Inclusion/Exclusion Criteria

General Inclusion Criteria

1. ≥18 to ≤80 years of age (male or female) at time of surgery
2. Patient has one of the following indications for open surgery based on CTA completed within 90 days of informed consent:
   - Acute, subacute, or chronic dissection that involves the aortic arch and the descending thoracic aorta, with or without involvement of the ascending aorta
     - Note: If a dissection patient also has an aneurysm, they should be enrolled as a dissection patient.
   - Aneurysm that involves the aortic arch and the descending thoracic aorta, with or without involvement of the ascending aorta
3. Patient, or patient's legally authorized representative (LAR; in the secondary arm only), provides written informed consent prior to any study procedures
4. Patient's surgery occurs within 90 days of informed consent

Anatomical Inclusion Criteria

5. Aortic diameter at the intended Arcevo™ LSA anastomosis site is ≥21 mm
6. For Aneurysm with distal sealing (i.e., single stage procedure), aortic diameter at the intended distal sealing zone is between 20-36 mm
7. For Dissection with distal sealing, aortic diameter at the intended distal sealing zone is between 22-40 mm
8. LSA branch does not require additional stenting further into the LSA (beyond the Arcevo™ LSA)
9. The intended LSA sealing zone has a diameter between 8.5 mm and 14.0 mm with a length of at least 10 mm
10. Absence of dissection, aneurysm, or stenosis in the intended LSA sealing zone
11. The intended LSA branch position does not interrupt flow to any branch vessel (e.g., left vertebral artery)
12. Patient does not have CT evidence of extreme arch or LSA angulation precluding safe passage of the Arcevo™ LSA and delivery system
13. LSA take-off angle between 15° and 90°
14. For patients requiring planned extension, there is a ≥ 2 cm distal seal zone for the TEVAR device without a severely angulated descending aorta
15. For patients requiring planned extension, patient has suitable iliac artery anatomy for safe passage of the TEVAR delivery system



8. The patient's surgery must occur within how many days of informed consent?

General Exclusion Criteria

1. Patient is pregnant, or planning to become pregnant during the course of the study; individuals of child-bearing potential must agree to use acceptable methods of contraception during the study
2. Patient has another medical condition (aside from the arch disease) that, in the opinion of the investigator, reduces the patient's life expectancy to <2 years
3. Patient has an existing aortic stent graft device in the descending aorta that would interact with Arcevo™ LSA
4. Patient has a medical, social, or psychological problem that, in the opinion of the investigator, could impede the patient's ability to return for follow-up
5. Patient is unwilling or unable to comply with the follow-up schedule
6. Patient is institutionalized due to administrative or judicial order
7. Patient is unwilling to accept blood transfusion or blood product
8. Patient is currently participating in another interventional clinical study which includes treatment with another investigational product (e.g., device, pharmaceutical, or biologic)

Medical Exclusion Criteria

9. Patient is unfit for open surgical repair involving circulatory arrest
10. Patient is in extreme hemodynamic compromise requiring CPR or substantial inotropic support prior to surgery
11. Patient has an active systemic infection
12. Patient has endocarditis or active infection of the aorta
13. Patient has a freely ruptured aorta
14. Patient has a history of a bleeding disorder (e.g., hemophilia)
15. Patient has current end-stage renal disease (e.g., GFR <30 mL/min)
16. Patient has a known allergy to Arcevo™ LSA components and TEVAR device components (if required) (nitinol, polyester, platinum-iridium, or polyethylene)
17. Patient has uncontrollable anaphylaxis to iodinated contrast or other inability to obtain CT angiograms during follow-up
18. Patient has acute coronary malperfusion
19. Patient has symptomatic visceral malperfusion

Who is Eligible?

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Case Examples

- The following 5 case examples are meant to test your memory and understanding of the ARTIZEN eligibility criteria
    - Feel free to reference the protocol and/or materials available at your table
- For each case, please use the Slido survey to make the appropriate response of ‘Eligible’ or ‘Not Eligible’
- If you think the patient doesn’t meet the eligibility criteria, please call out or message (if virtual) the reasons not eligible, when prompted

Case Example #1 – Eligible or Not?

Case:

A 71-year-old woman with a known stable ascending aortic aneurysm, measuring 4.6 cm about 1 year prior, presented at the hospital with acute chest pain, right leg paralysis, and acute epigastric pain. Her medical history is significant for hypertension, dyslipidemia, asthma, hypothyroidism, previous orthopedic surgery, and a hysterectomy. Imaging revealed an acute type A aortic dissection (ATAAD) extending from the aortic valve to the iliac bifurcation, with some radiographic evidence of visceral malperfusion (however, no present symptoms). The surgeon would like to urgently perform a total arch replacement (TAR) with frozen elephant trunk (FET). Concurrently, the patient also needs a bio-Bentall procedure for aortic root replacement.

9. Case Example #1

Case Example #1 – Eligible

Decision:

- While the patient does have some radiographic evidence of visceral malperfusion, only **symptomatic visceral malperfusion is an exclusion criterion**.
- The patient has an allowed procedure indication.
- The patient's age is within the 18-80 range.
- Previous procedures are allowed.
- Concomitant procedures are allowed.

Case Example #2 – Eligible or Not?

Case:

A 45-year-old male presented with a complaint of syncope, chest pain, and tachycardia. The patient is a current smoker, has a history of hypothyroidism, connective tissue disorder, chronic kidney disease, and a previous cholecystectomy procedure. CT imaging demonstrated an aortic aneurysm, with a max diameter of 7.3 cm involving the arch and the descending aorta. The surgeon has decided that this will be a single-stage TAR procedure + FET with distal sealing and measured the distal sealing zone as 38 mm. The patient will need a concomitant CABG procedure as well.

10. Case #2 - Eligible or Not?

Case Example #2 – Not Eligible

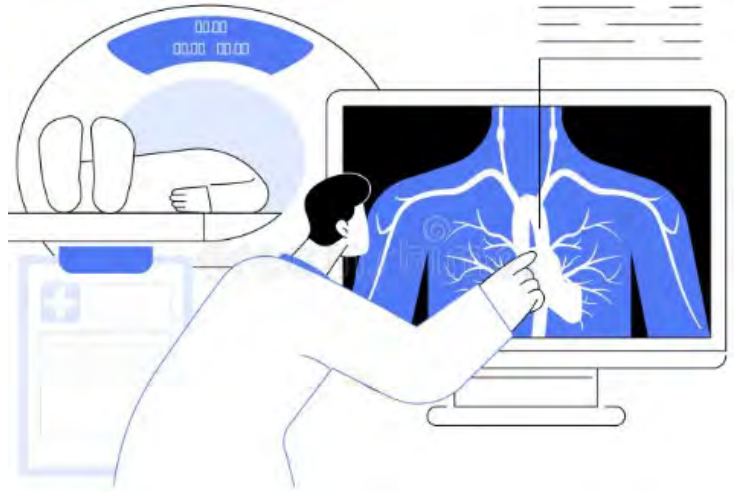
Decision:

- The patient is not eligible due to a 38 mm distal sealing zone.
  - o “For Aneurysm with distal sealing (i.e., single stage procedure), aortic diameter at the intended distal sealing zone is between **20-36 mm**”
- The patient has an allowed procedure indication.
- Having a connective tissue disorder is allowed.
- Chronic kidney disease is allowed.
  - o Current end-stage renal disease (e.g., GFR <30mL/min) is an exclusion criterion
- Concomitant CABG is allowed.

Case Example #3 – Eligible or Not?

Case:

A 25-year-old female presented to the ED with a 2-day history of chest pain. CTA revealed a nonA-nonB aortic dissection as well as a severely angulated descending aorta. She is in good health otherwise, and was trying to become pregnant but is willing to put that on hold for study duration and take contraceptives. The surgeon will perform a TAR + FET and the patient will also need a TEVAR implanted during the index procedure. Due to the angulation of the descending aorta, the distal seal zone for the TEVAR device would be 1.5 cm.



11. Case Example #3 - Eligible or Not?

Case Example #3 – Not Eligible

Decision:

- The patient is not eligible due to the severely angulated descending aorta and only 1.5 cm distal seal zone for the TEVAR device.
    - o “For patients requiring planned extension, there is a **>2 cm distal seal zone** for the TEVAR device **without a severely angulated descending aorta**.”
- Patient is within the acceptable age range.
- The patient is willing to take contraceptives to be in the study.

Case Example #4 – Eligible or Not?

Case:

An 82-year-old male has complaints of shortness of breath on exertion for about 2 years. More recently, he experienced frequent left back pain. He is a current smoker, takes medication for high blood pressure, high cholesterol, has stage 2 chronic kidney disease, has a history of ischemic stroke 1 year ago, and will require a concomitant aortic valve replacement. The patient's wife mentions that the blood pressure medication he is taking is part of an investigational study. A CT scan showed an aortic arch aneurysm. The surgeon would like to perform a TAR + FET.

12. Case Example #4 - Eligible or Not?

Case Example #4 – Not Eligible

Decision:

- The patient is not eligible due to currently participating in another interventional clinical study which includes treatment with another investigational product (e.g., device, pharmaceutical, or biologic).
- The patient is also not eligible due to his age being >80 years old.
- The patient has an acceptable procedure indication.
- Concomitant procedures are allowed.

Case Example #5 – Eligible or Not?

Case:

A 76-year-old male presented with sudden, sharp pain in the chest, which radiates to the back, neck, and jaw. Imaging reveals that he has a chronic aortic dissection, affecting the arch, as well as a penetrating aortic ulcer (PAU). He had a stroke 2 years ago and currently has COPD, which is stable and managed with medication. Previous procedures include CABG and mitral valve repair. The surgeon would like to perform TAR + FET. The patient's aortic diameter at the intended distal sealing zone is 34 mm and the LSA branch does not require additional stenting (past the 40 mm LSA stent). The LSA sealing zone is 12 mm and the LSA take-off angle is 20°.

13. Case Example #5 - Eligible or not?

Case Example #5 – Eligible

Decision:

- Patients may have >1 aortic disease present in addition to their main indication for treatment (i.e., intramural hematoma (IMH), or penetrating aortic ulcer (PAU)).
- Prior stroke is allowed
- Previous procedures are allowed.
- The aortic measurements are acceptable.
  - For dissection with distal sealing, aortic diameter at the intended distal sealing zone = 22-40 mm".
  - LSA branch does not require additional stenting further into the LSA.
  - Intended LSA sealing zone diameter between 8.5 -14.0 mm, with a length ≥10 mm.
  - LSA take-off angle between 15° - 90°".

Break

Monitoring and Site Responsibilities

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Monitoring Strategy

Monitoring Strategy:

- Routine interim monitoring visits (IMVs) will be performed by an **Artivion clinical research associate (CRA)** per the Clinical Monitoring Plan (CMP) to assess the Investigator's adherence to the protocol, IRB requirements, maintenance of records and reports, and review of source documents for accuracy, completeness, legibility, and omissions.
- The monitoring strategy includes **100% source document verification (SDV) of all informed consents** (including screen failures) and 100% SDV (for all visits) for the first two subjects enrolled at each site.
- The following will be **100% monitored for all enrolled patients**:
  - All eligibility criteria
  - Procedure eCRFs
  - Serious adverse events (SAEs) and AEs of interest (i.e., events defined as primary and/or secondary endpoints)
- Additional subjects and forms may be monitored at a reduced schema

Monitoring Strategy (cont.):

The following documents and/or information is considered critical and will be reviewed at IMVs:

- Informed Consent
- Eligibility Assessment
- Demographics
- Baseline Assessment (demographics, medical history)
- Lab Tests (i.e., βhCG pregnancy and creatinine)
- Procedure (including cross checking to ensure procedure is ≤90 days from ICF)
- Device Technical Success
- Imaging evaluation (site entry only and to ensure all fields are entered)
- Modified Rankin Scale
- Modified Tarlov Scale
- Additional Post-Operative Procedures (in the event of an aortic procedure)

Monitoring Expectations:

- CRAs will complete the following during IMVs:
  - Source document review
  - SDV (based on pre-defined strategy)
  - Regulatory binder review
  - Device accountability
- It's expected that the CRA is given access to the site's electronic medical record (EMR) or paper source, regulatory binder, and patient binders.
  - If they site has any special requirements or forms that need to be submitted prior to access being received, please let your CRA know at time of site activation to prevent issues with access.
  - In cases where the site cannot grant the CRA direct EMR access, the site staff must be available during the IMV to assist with patient data access and SDV, as needed (ex. over-the-shoulder viewing, print outs, etc.).
- The PI is expected to be available at some point during the IMVs
  - IMVs should be scheduled around PI availability and if PI is unable to make the IMV, a follow-up call should be scheduled.
- IMVs are intended to be conducted **on-site** but may be performed remotely when necessary.
- Study team will be notified of the progress of any outstanding or ongoing study issues by the Lead CRA/monitor.

Monitoring Expectations (cont.):

- After the site coordinator and Artivion CRA agree on an IMV date, the CRA will e-mail the PI and coordinator to confirm the date; this e-mail will serve as your **confirmation notification** and should be saved in your Regulatory binder.
- Within 20 business days of the IMV, your CRA will send you an e-mail with an attached **follow-up letter**, which will include a summary of activities completed and a list of any action items.
  - If you have any questions on the content of the letter, you should follow-up with your CRA
  - The follow-up letter should be saved in your Regulatory binder.
- All efforts should be made between the CRA and the site coordinator to resolve action items during the IMV, or shortly thereafter.
  - Ad hoc phone calls or correspondance can be used to address simple questions between IMVs
  - Coordinator should respond in a timely manner (<48 business hours) to clarify data or provide additional documentation
- Data collected at any satellite sites will be reviewed at the main study site via remote monitoring.
  - If the site does not have centralized medical records data will be reviewed at the satellite location.

Monitoring Expectations (cont.):

- The following logs should be reviewed and updated prior to an IMV:
  - Site Delegation and Authority Log
  - Device Accountability Log
  - Site Screening and Enrollment Log
  - Protocol Deviation Log
  - Adverse Event Log (site specific template)
- All study staff must complete required study training prior to being added to the Site Delegation and Authority Log
- Sites are required to maintain signed/dated training logs in Regulatory Binder.
- Updates to delegation log must reflect current study responsibilities and must be initialed by the PI (in a reasonable amount of time)

Monitoring Visit Schedule

Monitoring Schedule:

- A site's 1st IMV will occur within **21 business days** after the 1st subject enrollment (i.e., Arcevo LSA implantation date) and then will occur periodically, throughout the study follow-up period.
- Monitoring will be more frequent during enrollment and through 1-year follow-up.
  - IMV frequency will be based on
    - Quantity of data to be monitored/reviewed
    - Outstanding action items or triggers/issues resulting from centralized data review
    - Status of data entry accuracy and timeliness
    - Device accountability accuracy and timeliness
    - # AEs and SAEs
    - # of protocol deviations
- Each site with at least 1 enrollment will be monitored at least **annually**.
- If a device deficiency is report, an IMV will occur within **21 business days** of Sponsor awareness.

Site Responsibilities

Site Responsibilities:

- Screening patients for eligibility and tracking in pre-screen log and Site Screening and Enrollment Log
- Obtaining and documenting informed consent for eligible subjects
- Timely and accurate data collection and entry
- Device accountability for Arcevo LSA
- Continued efforts to ensure subject retention and visits scheduled within anticipated windows
- Regulatory Binder maintenance (binders provided by Artivion)
- Subject binder maintenance (binders provided by Artivion)
- Accurate reporting of Adverse Events in the EDC
- Maintain confidentiality
- Obtain and maintain IRB approval
- Completion (and maintenance, as required) of all study-required training
- Completion of required Case Review and Support activities
- Connecting with Medtronic Sales Reps for TEVAR training, case support and questions, as needed
    - Medtronic has requested that your sales rep attend any cases

PI Responsibilities:

- Protect the rights, safety, and welfare of patients
- Adverse event severity and relatedness assessments
- Ensure data entry and accuracy
- Return remaining supply of the investigational product at the sponsor’s request
- Store study data for the required retention period
- Authorization of appropriately trained/qualified personnel on DOAL
- Provide accurate financial information to sponsor at the beginning of study and as requested
- Restrict access and use of the investigational device to authorized personnel and for eligible patients
- Facilitate execution and maintenance of CTA and Investigator Agreements prior to the study start
- Conduct the investigation in accordance with the signed agreement with the sponsor, the protocol, CTA

Common Findings & Best Practices

Common Audit Findings:

- Missing PI signatures on source or eCRFs
- Late AE or SAE reporting
- Incomplete device accountability logs
- Delayed or inaccurate data entry
- Missing/incomplete source documents

Best Practices:

- Schedule regular PI review/sign-off sessions
- Assign specific individuals AE entry responsibilities, including back-ups in the event your primary person is out, and enter minimal information as quickly as possible
- Update device accountability log for each shipment received and at time of each use
- Stay on top of data entry, with a goal of entering information into EDC within 3 business days; if you know there will be a delay in critical data, please communicate this to your CRA
- Maintain well-organized source documentation and utilize the provided worksheets, as needed

Common Findings & Best Practices (cont.)

You can also avoid the findings by completing the following prior to an IMV:

- Organize Regulatory Binder and ensure documents are current (IRB approvals, delegation log, training records)
- Reconcile and prepare Device Accountability Logs
- Ensure source documentation is complete and available
- Update Delegation of Authority Log with signatures
- Confirm PI/Sub-I availability for required discussions
- Ensure all outstanding queries are addressed before visit

Communication & Escalation Path

- In the event there is a site issue related to data entry, patient follow-up, protocol deviations, IMVs, SAE reporting, change in study staff, essential document collection, etc. your primary point of contact is your CRA or the lead CRA.
  - Your CRA may escalate to the Artivion PM as needed
  - For SAE issues and events requiring adjudication, the CRO (Bright Research) will also be involved
- In the event there is a site issue related to billing, investigational product shipment/receipt/ invoicing, contracts, site training, eligibility questions, etc. your primary point of contact is your Artivion PM
- In the event of time sensitive issues, such as unanticipated device-related SAEs or device deficiencies → immediate notification and/or follow-up is required.

Case Scenario & Discussion

The following are a few examples of common monitoring scenarios. Please answer the questions using Slido.

1. During an IMV, the CRA discovers that the first subject enrolled was hospitalized and the date the SAE was reported to the Sponsor was 10 days after site awareness.

14. What is the potential impact of delayed SAE reporting on patient safety and study compliance?

15. What can the site do to prevent recurrence?

Case Scenario & Discussion (cont.)

The following are a few examples of common monitoring scenarios. Please answer the questions using Slido.

2. Before an IMV, the CRA discovers that the second subject's most recent AE is missing an assessment of causality to Arcevo LSA. The site awareness date is 60 days ago.

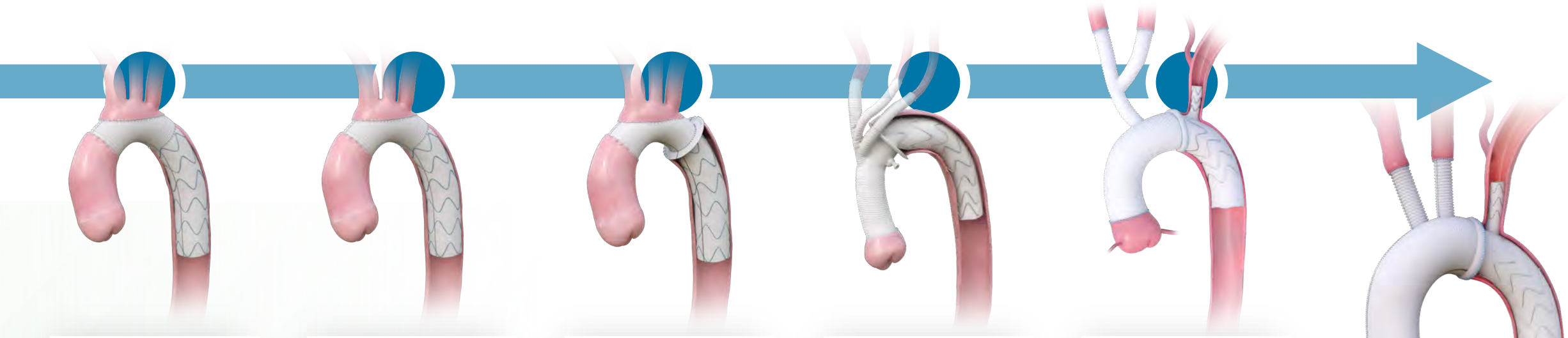
16. What is the potential impact of this finding?

Previous Clinical Experience in Europe and the US

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

European Experience with E-vita OPEN NEO

20 Years of Innovation in Aortic Arch Management



2005

FIRST CASES E-VITA® OPEN PERFORMED IN ESSEN GERMANY

2008

E-VITA® OPEN PLUS INTRODUCED

2012

E-VITA® OPEN PLUS MODIFIED

2020

E-VITA® OPEN NEO LAUNCHED

2025

NEO EDE™ LAUNCHED

2029

Arcevo™ LSA

Clinical Experience

- No prior clinical use of the current Arcevo™ LSA device; this is a first-in-man study
- 3 Post-Market Studies of E-vita OPEN NEO (prior iteration of Arcevo LSA):
  - NEOS (NCT04676672)
    - **# Patients Enrolled**: 163
    - **Status**: Follow-up
    - **Geography**: Austria (n=58) and Germany (n=123)
  - NEOS APAC (NCT04986709)
    - **# Patients Enrolled**: 116
    - **Status**: Follow-up
    - **Geography**: Australia, Hong Kong, Republic of Korea, Malaysia, Singapore, Thailand
  - NEO (NCT05721001)
    - **# Patients Enrolled**: 130
    - **Status**: Follow-up
    - **Geography**: France

Clinical Data from the NEOS Study

The 1st interim results from the NEOS Study Reported the following[1]:

Baseline Data:

- 100 patients enrolled between 12/2020 - 3/2022 at 12 centers in Europe and Hong Kong
- 66.7% male; mean age of 57.7 years
- Indications:
  - 37 patients with acute/subacute dissection
  - 33 with chronic dissection
  - 29 with aneurysm

Clinical Outcomes (up to 6-months post-op):

- High Technical Success (97%)
- Low 30-Day Mortality Rate (5%)
- Low New Disabling Stroke Rate (4%)
- Low Renal Failure/Dialysis Rate (3%)
- Low Paraplegia and Paraparesis Rate (2%, respectively)

Pre-op CT image. Distal aortic arch aneurysm with a dissection and contrast media invading the false lumen (arrow).

Post-op CT image. Complete sealing of the entry tear by the E-vita OPEN NEO Stent Graft System

[1]Tsagakis K, Kempfert J, Zierer A, Martens A, Dohle DS, Castiglioni A, Wong RH, Widenka K, Liakopoulos O, Borger MA, Oo AY, Holubec T, Luehr M, Legarra Calderón JJ, Grabenwöger M. E-vita OPEN NEO in the treatment of acute or chronic aortic pathologies: first interim results of the NEOS study. Eur J Cardiothorac Surg. 2024 Jun 3;65(6):ezae206. doi: 10.1093/ejcts/ezae206. PMID: 38830042; PMCID: PMC11162351.

ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

European Experience with Extra Design Engineering (EDE)

Neo EDE™ Hybrid Arch Device

Custom-Made FET Device

June 2025
NEO EDE™
LAUNCHED

Neo EDE™ allows the physician to fully customize Artivion's FET portfolio for patients with aneurysm and/or dissection in the aortic arch by:

- Customizing the Stent Graft (length, diameter, distance collar to Outer Branch)
- Customizing the Vascular Graft (vas. graft length, configuration of vas. branches)
- Customizing the Suture Collar (straight, conical, angled)

➢ Customized within 22 working days after official order is generated

Recommended use:

- Supra aortic vessel diameter must be 8.5 mm – 14 mm at a depth of 30 mm past the ostium
- Angulation of Outer Branch min. 15º - max. 90º
- Distance to Vertebral Artery (from LSA) ≥ 40 mm

Not recommended use:

- Severe angulated LSA (< 15º / > 90º)
- Distance between LSA ostium to LVA < 30 mm

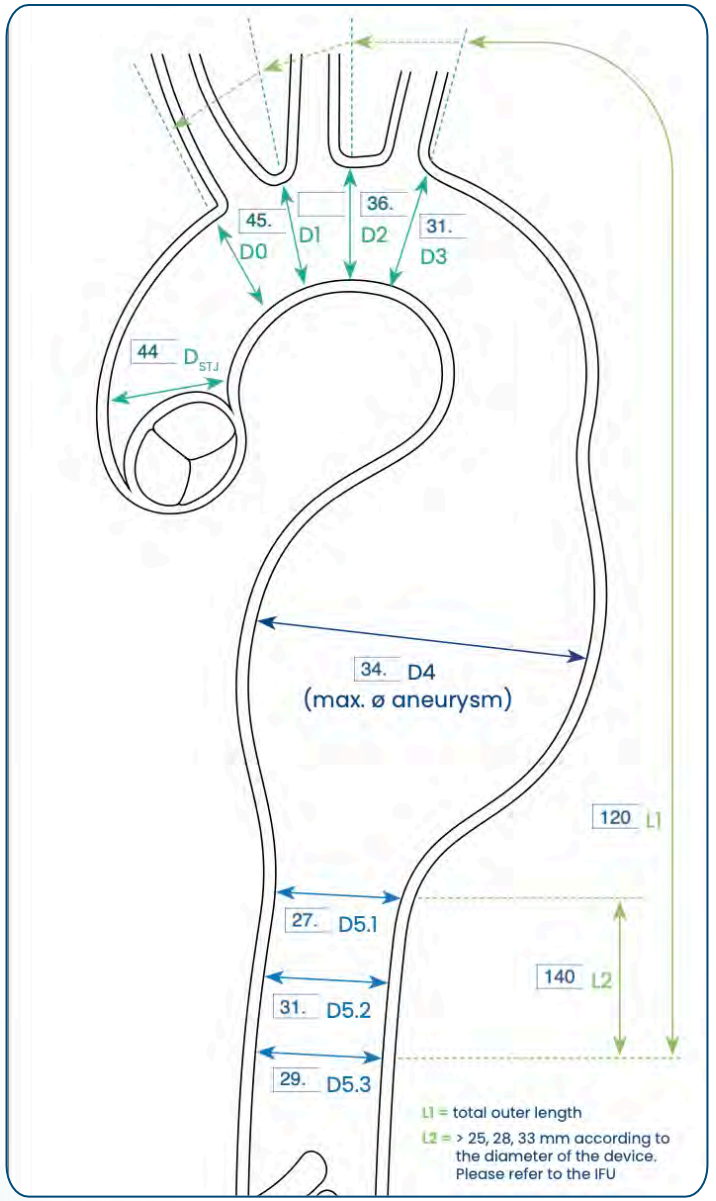
Case Details: Pre-operative DICOM

Indication for Treatment: Aortic Aneurysm of the Ascending, Arch and Proximal thoracic aorta

ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Case Details: Aortic Arch - Measurements

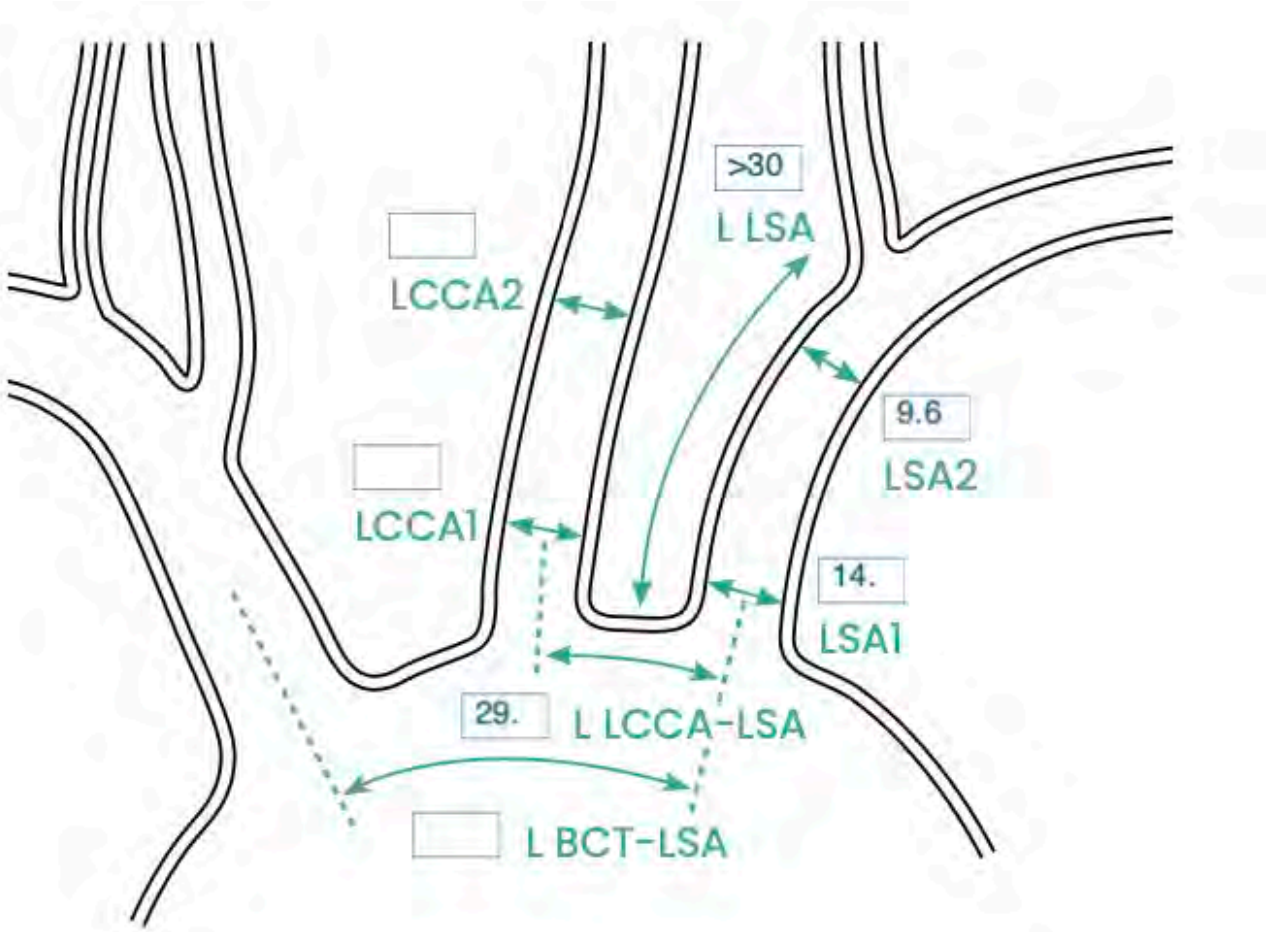
- Ascending Aorta: 45 – 47mm
- Aortic Arch: 31 – 35mm
- Descending Aorta: 30 – 35mm



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Case Details: LSA Measurements

- The LSA starts at 14.2 mm then narrows down to 11.3mm at 1.5cm and 9.6 mm at 3 cm.
- Therefore, to make sure we get a good seal we will use the 15 mm LSA stent.
- The left vertebral artery (LVA) is over 30 mm from the ostium of the LSA away, so the 40 mm length of the outer branch is fine.

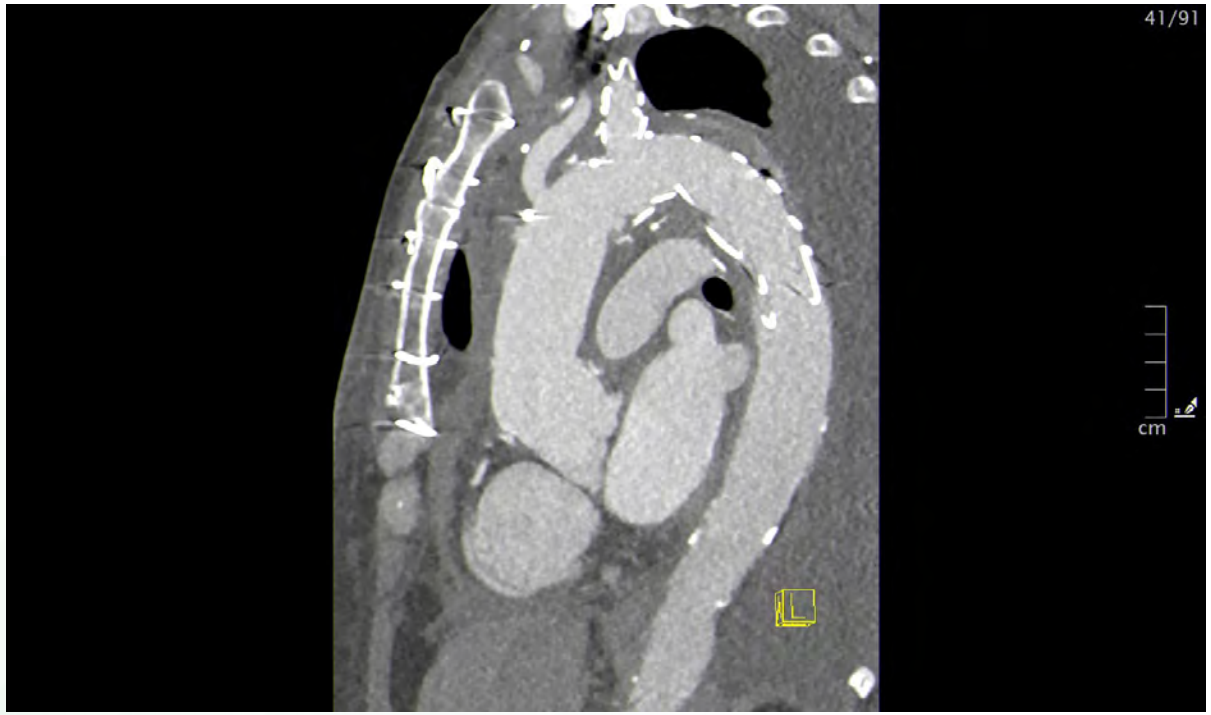


Technical Drawing

First NEO EDE Case Video

Post-Procedure Imaging

Post Op CT Scan



- **Question for the Committee**: Any questions on the case, implantation, or post-procedure results?

B-SAFER Experience

Device Training

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Device Introduction

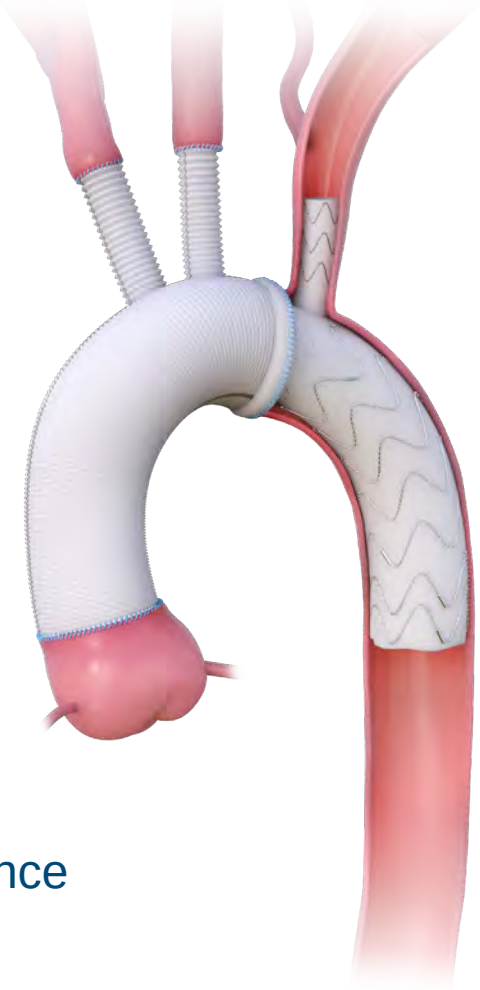
Indications and Use

Indications for Use:

- Arcevo™ LSA is indicated for use in patients with dissection and/or aneurysm involving the aortic arch and the descending thoracic aorta, with or without involvement of the ascending aorta.

Intended Use:

- Arcevo™ LSA is intended for the surgical treatment of patients with dissection and/or aneurysm involving the aortic arch and the descending thoracic aorta, with or without the involvement of the ascending aorta.
- Intended for attachment to a proximal surgical graft (not supplied).
- Patients who need additional stent graft coverage distally, may require extension with the Valiant™ Captivia™ (not supplied) after the initial index procedure using the IFU provided for that device.
- Arcevo™ LSA is intended to be used by trained cardiothoracic surgeons with experience in performing aortic arch procedures in a surgical suite or in the operating room.

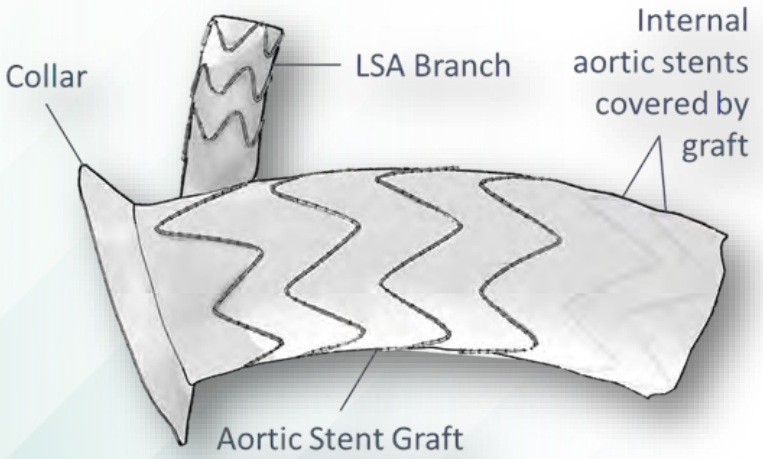


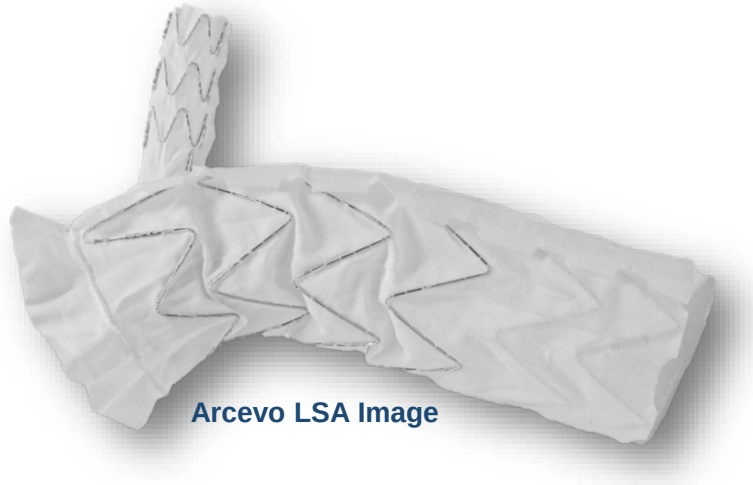
Contraindications:

- Patients with known sensitivities or allergies to nitinol, platinum-iridium, polyester, and/or polyethylene, in patients with systemic infection, and in patients with endocarditis or active infection of the aorta.

Arcevo LSA Overview

- Designed with an aortic stent graft body and stented LSA branch.
- Made of self-expanding nitinol aortic stents attached to polyethylene terephthalate (PET or polyester) graft material using ultra-high molecular weight polyethylene (UHMWPE) sutures.
- Proximal end has a conical shaped collar which is ~15 mm in length for anastomosis to the native aorta and a proximal surgical graft (not supplied by Artivion).





Arcevo LSA Image

17. Artivion is supplying the proximal surgical graft for this study.

Aortic Stent Design

- **Conical Collar**
  - Conical collar for secure anastomosis to native aorta
  - Collar diameters range from 50-65 mm
- **Aortic Stent Graft**
  - Available in a 24-40 mm diameter range with 120 mm or 130 mm lengths
  - Z-Stents
    - 3-4 External sewn Nitinol Z-stents distal to LSA branch
    - 2 Internal sewn Nitinol Z-stents at distal end
- **Radiopaque Markers**
  - 1 RO ring marker at distal end of the LSA branch
  - 3 RO ring markers triangulated around the LSA stent graft
    - 2 RO markers proximal to the LSA branch on aortic graft
    - 1 RO marker distal to LSA branch on aortic graft
  - 1 RO ring marker at distal end of the Arcevo LSA stent graft

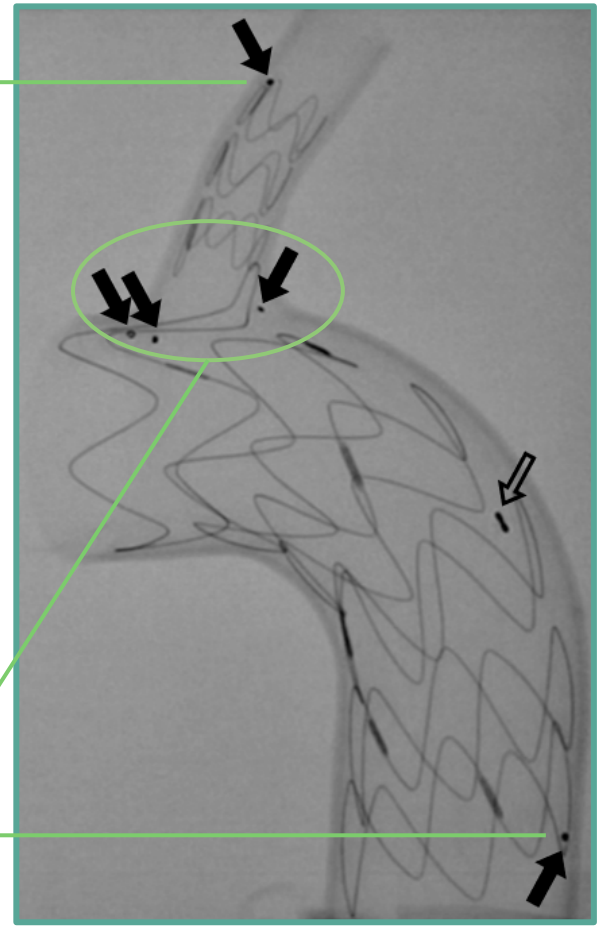
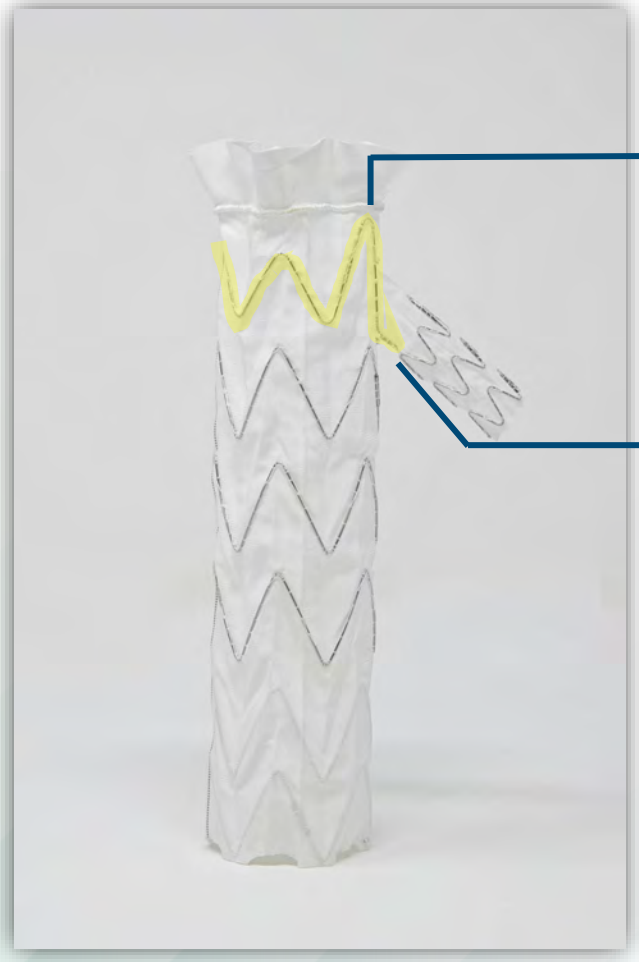


Image of Arcevo LSA ring radiopaque markers (solid arrows) and overlap radiopaque marker (open arrow) for distal extension with thoracic stent graft

LSA Branch Stent Design

- 40 mm stent length into the LSA
- 70° branch take-off angle
- 3 Z-stent rings with radial force to promote robust sealing
- 11 mm and 15 mm stent diameters to fit vessels from 8.5 mm to 14 mm
- 10 mm to 12 mm distance between suture collar and stented branch

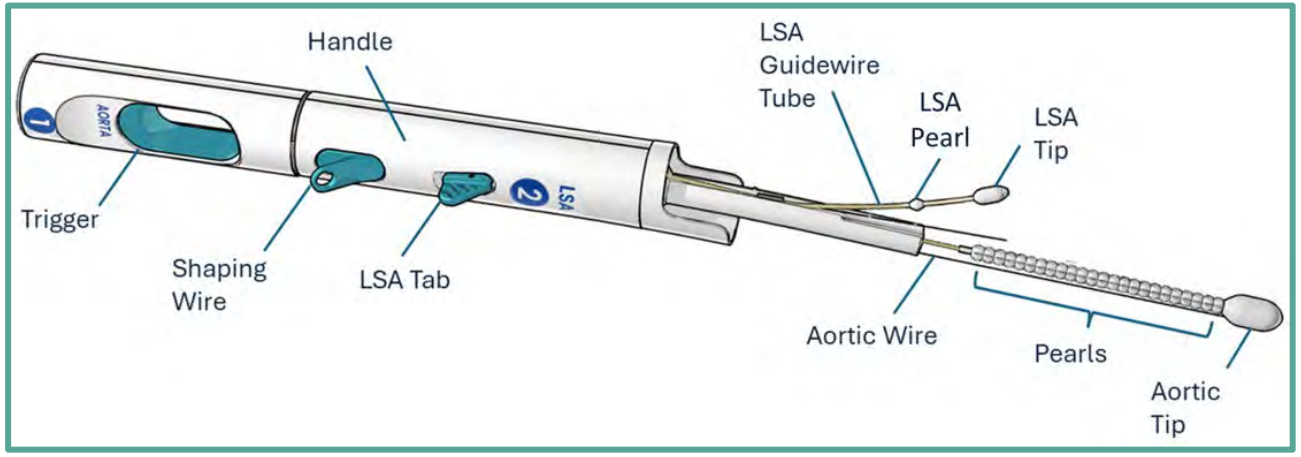
Backstop Spring Design

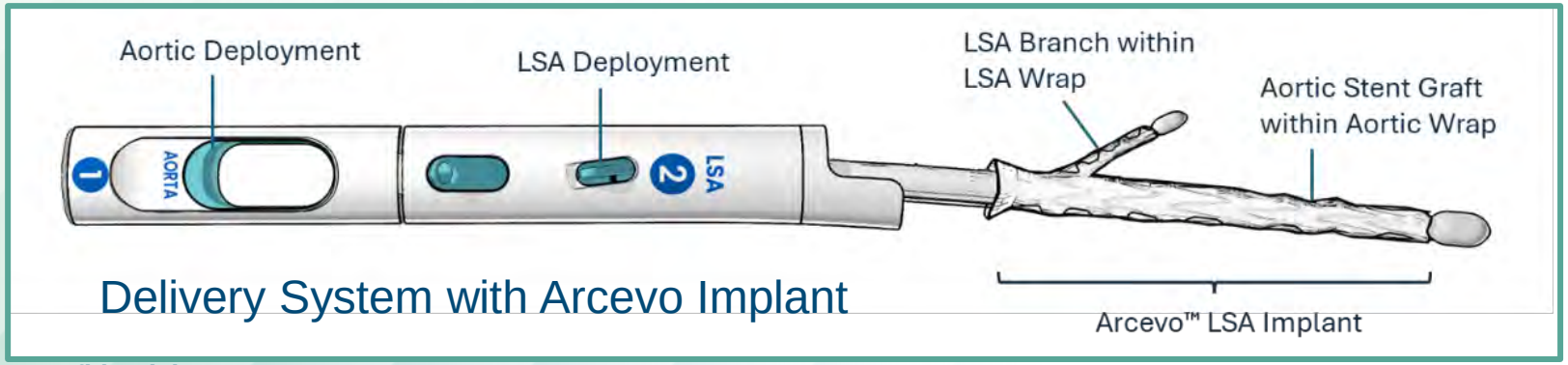


- Z stent closest to the collar has longer apices on the greater curve and shorter apices on the lesser curve which provides for a more natural conforming fit of the device within the curved segment of the arch
- Backstop peak below LSA branch
  - Provides support for LSA branch to ensure lumen patency
  - Facilitates proper positioning and axial alignment of branch in native LSA vessel

Delivery System

- Includes aortic and LSA sections connected to the handle for insertion, positioning, and deployment into the aorta.
- Each section is comprised of polyether ether ketone (PEEK) guidewire tube ending in an atraumatic aortic tip.
- The aortic guidewire tube is threaded with pearls to provide a surface for crimping of the stent graft (LSA branch has 1 pearl).
- If an aortic guidewire is not used, a flexible shaping wire is provided to add delivery system support during implant pre-shaping, insertion, and deployment.

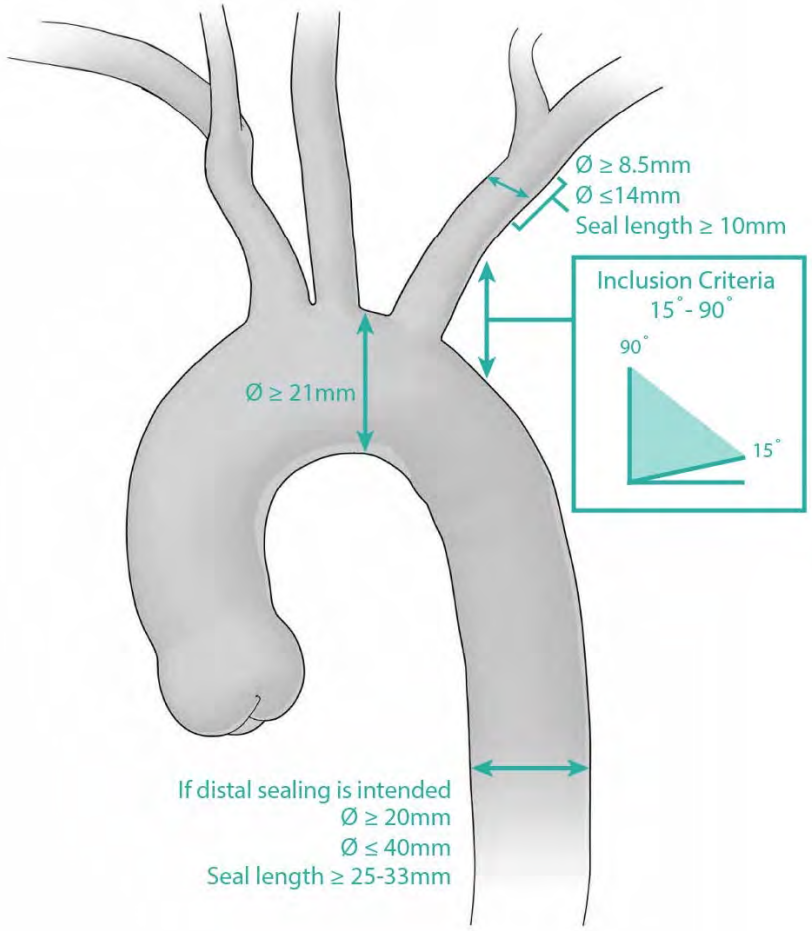




Delivery System with Arcevo Implant

Arcevo LSA Sizing Basics

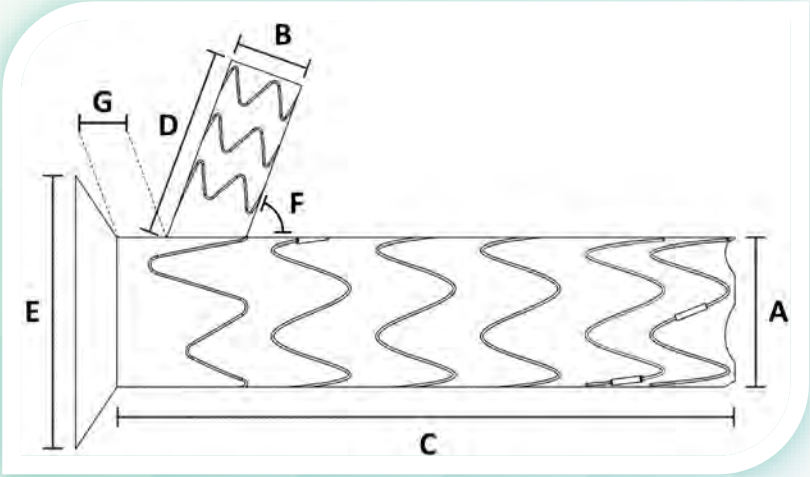
- Computed tomography angiography (CTA) is required to accurately assess patient anatomy prior to treatment.
- Physicians should evaluate each patient to determine if the Arcevo LSA implant is appropriate.
- A patient must meet the following basic criteria to be considered (see figure on the right):
  - Aortic diameter in zone 2 (proximal to LSA) is ≥21 mm
  - LSA Takeoff angle from aorta between 15-90 degrees
  - LSA seal zone with a length of ≥10 mm and diameter between 8.5-14 mm
  - If distal sealing is intended, seal zone with length of ≥25-33 mm (stent size dependent) and diameter between 20-40 mm



Acceptable Aortic Morphology for Arcevo LSA Patient Selection

Arcevo LSA Sizing Options and Measurements

- There are 11 device configurations
- Aortic diameter ranges between 24-40 mm
- Aortic length is 120 or 130 mm depending on the device diameter
- There are 2 LSA diameter options (11 and 15 mm)
- There is 1 LSA length (40 mm)
- See figure below and table to the right for additional details



Arcevo LSA Model	[A] Aortic Diameter (mm)	[B] LSA Diameter (mm)	[C] Nominal Aortic Length* (mm)	[D] Nominal LSA Length* (mm)	[E] Collar Diameter (mm)	[F] LSA Branch Angle (°)	[G] Collar to Branch Length (mm)
ARC-A24-B11	24	11	120	40	50	70	10
ARC-A26-B11	26	11					10
ARC-A28-B11	28	11			55		12
ARC-A28-B15	28	15					10
ARC-A30-B11	30	11					12
ARC-A30-B15	30	15					10
ARC-A33-B11	33	11	130		60		12
ARC-A33-B15	33	15					10
ARC-A36-B11	36	11					12
ARC-A36-B15	36	15					10
ARC-A40-B15	40	15			65		10

*Nominal aortic lengths range from 119-124 mm for 120 mm devices and 132-134 mm for 130 mm devices. Nominal LSA branch lengths range from 40-44 mm.

Arcevo LSA Sizing and Placement

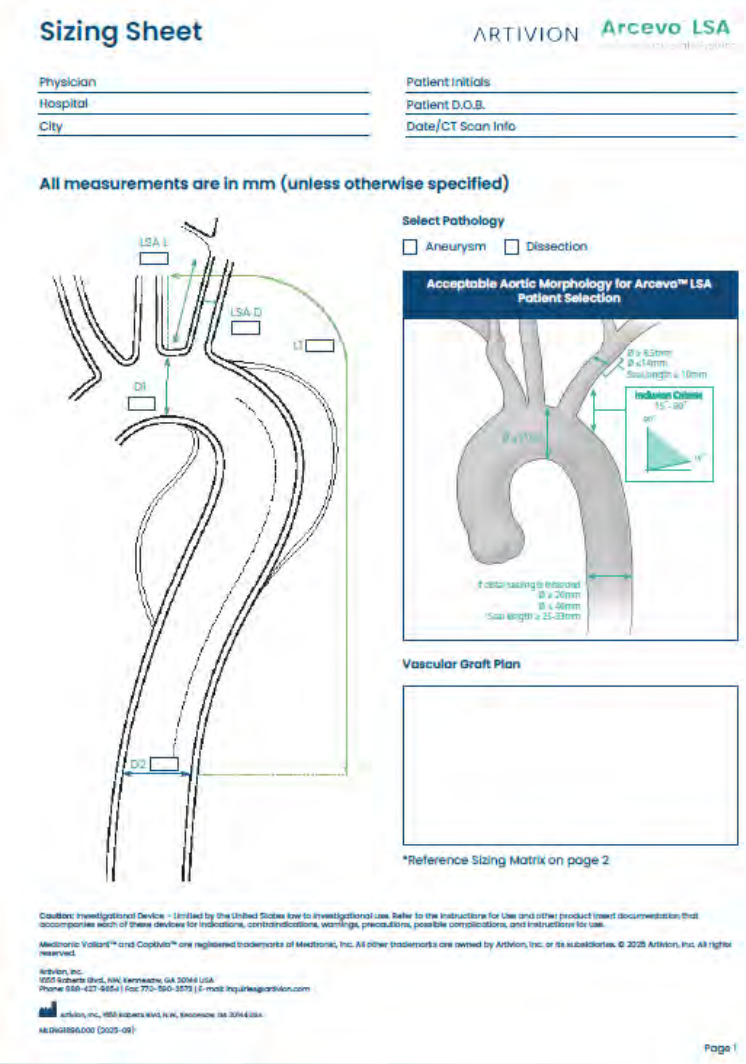
Stent graft device should be selected based on the sizing guidelines (table below) as well as the complete treatment strategy, including the size of the distal landing zone of the TEVAR device, if needed.

Arcevo™ LSA Model	All Indications:		If Distal Sealing is Intended (no TEVAR):		
			Aortic diameter at the intended Arcevo™ LSA distal sealing zone (mm)		Minimum length of seal zone (mm)
	Aortic diameter at the intended Arcevo™ LSA proximal anastomosis site (mm)	LSA Diameter Range (mm)	Aneurysm*	Dissection**	
ARC-A24-B11	≥ 21	8.5 – 14.0	20 – 22	22 – 24	25
ARC-A26-B11	≥ 23		22 – 24	24 – 26	28
ARC-A28-B11	≥ 25		24 – 25	26 – 28	
ARC-A28-B15					
ARC-A30-B11	≥ 26		25 – 28	28 – 30	
ARC-A30-B15					
ARC-A33-B11	≥ 29		28 – 30	30 – 33	33
ARC-A33-B15					
ARC-A36-B11	≥ 32		30 – 34	33 – 36	
ARC-A36-B15					
ARC-A40-B15	≥ 35		34 – 36	36 – 40	

*Sizing for aortic aneurysms with distal sealing were developed with approximate oversizing of 5-20% based on native aortic diameter ranges.
**Sizing for aortic dissections with distal sealing were developed with approximate oversizing up to 10% based on native aortic diameter ranges.

Arcevo LSA Sizing Sheet

Each site will be provided digital and physical copies of the device sizing sheet pictured in the images below. Please make these accessible to all implanting investigators.



Sizing Sheet

ARTIVION Arcevo LSA

Physician
Hospital
City

Patient Initials
Patient D.O.B.
Date/CT Scan Info

All measurements are in mm (unless otherwise specified)

Select Pathology

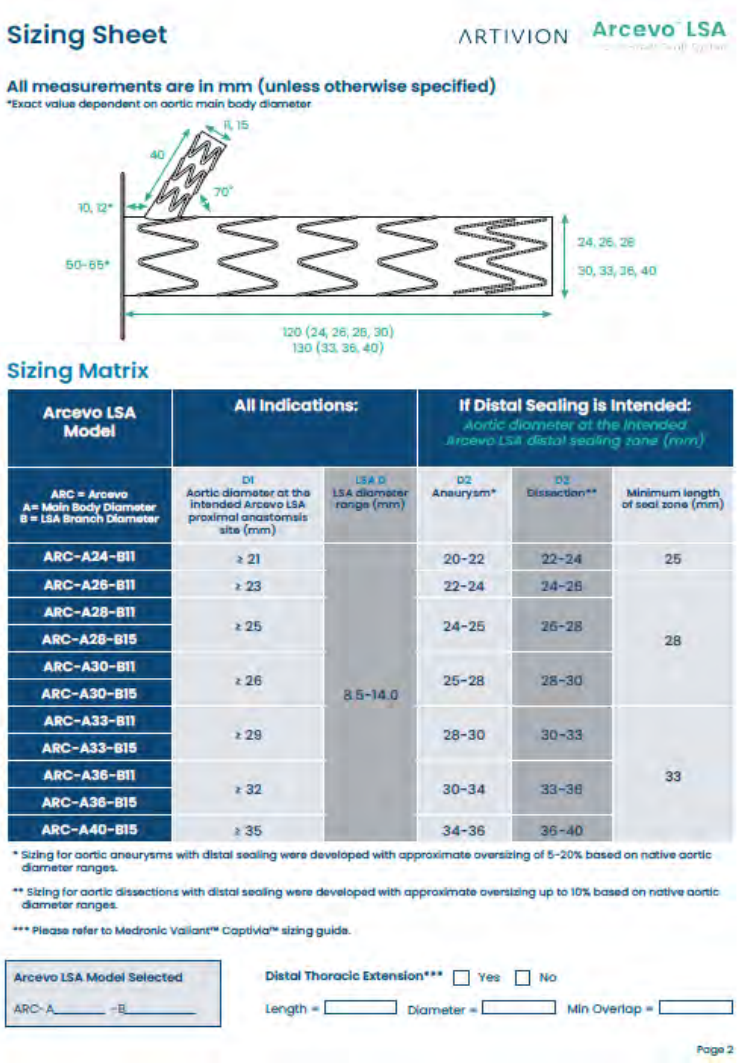
☐ Aneurysm ☐ Dissection

Acceptable Aortic Morphology for Arcevo™ LSA Patient Selection

Vascular Graft Plan

*Reference Sizing Matrix on page 2

Page 1



Sizing Sheet

ARTIVION Arcevo™ LSA

All measurements are in mm (unless otherwise specified)

*Exact value dependent on aortic main body diameter

Sizing Matrix

Arcevo LSA Model	All Indications:		If Distal Sealing is Intended: Aortic diameter at the intended Arcevo LSA distal sealing zone (mm)		
ARC = Arcevo A= Main Body Diameter B = LSA Branch Diameter	D1 Aortic diameter at the intended Arcevo LSA proximal anastomsis site (mm)	LSA D LSA diameter range (mm)	D2 Aneurysm*	D2 Dissection**	Minimum length of seal zone (mm)
ARC-A24-B11	≥ 21	8.5-14.0	20-22	22-24	25
ARC-A26-B11	≥ 23		22-24	24-26	28
ARC-A28-B11	≥ 25		24-25	26-28	
ARC-A28-B15					
ARC-A30-B11	≥ 26		25-28	28-30	
ARC-A30-B15					
ARC-A33-B11	≥ 29		28-30	30-33	33
ARC-A33-B15					
ARC-A36-B11	≥ 32		30-34	33-36	
ARC-A36-B15					
ARC-A40-B15	≥ 35		34-36	36-40	

* Sizing for aortic aneurysms with distal sealing were developed with approximate oversizing of 5-20% based on native aortic diameter ranges.

** Sizing for aortic dissections with distal sealing were developed with approximate oversizing up to 10% based on native aortic diameter ranges.

*** Please refer to Medronic Valiant™ Captivia™ sizing guide.

Arcevo LSA Model Selected
ARC-A_____-B_____

Distal Thoracic Extension*** ☐ Yes ☐ No
Length = ☐ Diameter = ☐ Min Overlap = ☐

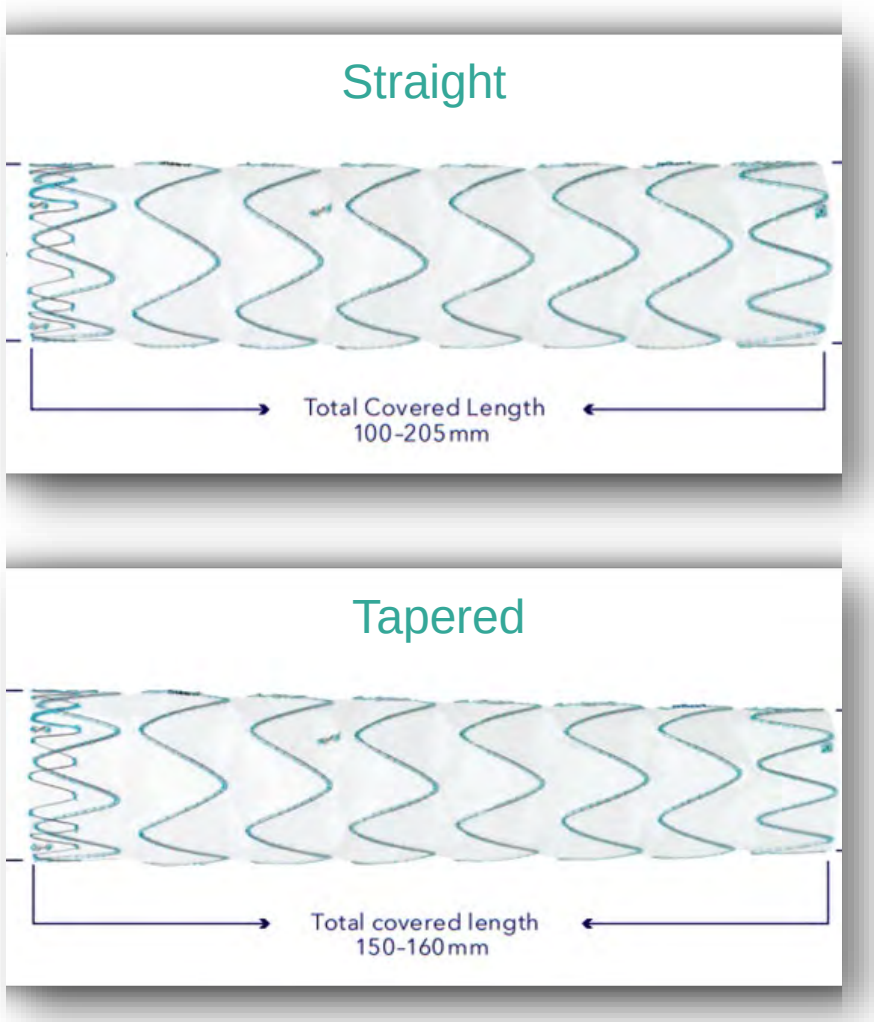
Page 2

Distal Extension Planning

- Prior to the index procedure, it's important for the implanting surgeon to determine whether or not the patient requires a thoracic endovascular aortic repair (TEVAR) to complete treatment
- The surgeon will document plans for any future aortic treatment on the following 2 fields in the Treatment Planning & Device Sizing eCRF:
  - "Is the treatment plan to complete treatment in a single stage (for current disease presentation)?"
  - "Do you anticipate additional aortic treatment in the future"
- Single stage procedures would most likely include acute dissection and localized aneurysms
- Multi-stage procedures may be considered in the following cases:
  - Distal end of the Arcevo LSA will land in unsupported aorta (i.e., in the aneurysm sac)
    - Therefore, there will be an expected Type 1B endoleak
  - Chronic dissection due to high likelihood of persistent FL perfusion
  - Anticipated later aortic enlargement (for any reason)

TEVAR Extension - Medtronic Valiant™ Captivia™ Information

- Closed Web, straight or tapered devices **are required** to extend Arcevo LSA and include only the following options:
  - o 24-44 mm proximal diameters
  - o 100-205 mm lengths
  - o All commercial stock, not an investigational product.
- See Medtronic Valiant™ Captivia™ IFU for sizing and other instructions
- Sites to contact their local Medtronic sales rep or clinical specialist for ordering information and/or questions regarding the Valiant™ Captivia™ device
- Medtronic representative to be included in Valiant TEVAR procedures



Arcevo LSA and Distal Extension Size Pairings

- Minimum required overlap length with Arcevo LSA: >50 mm
- 0% oversizing has not been tested in an unsupported aneurysm model

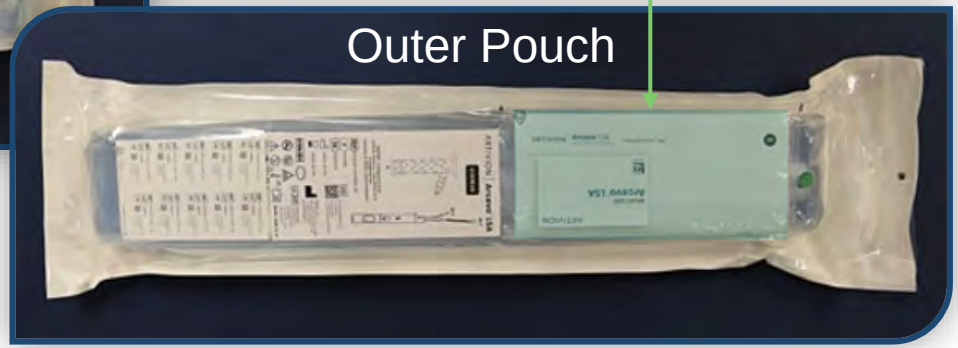
Arcevo LSA Model Number	Valiant™ Captivia™ Proximal Sizing
ARC-A24-B11	24 mm / 26 mm / 28 mm
ARC-A26-B11	26 mm / 28 mm / 30 mm
ARC-A28-B11	28 mm / 30 mm / 32 mm
ARC-A28-B15	
ARC-A30-B11	30 mm / 32 mm / 34 mm
ARC-A30-B15	
ARC-A33-B11	34 mm / 36 mm / 38 mm
ARC-A33-B15	
ARC-A36-B11	36 mm / 38 mm / 40 mm
ARC-A36-B15	
ARC-A40-B15	40 mm / 42 mm / 44 mm

Packaging and Labeling

- Arcevo LSA (implant loaded onto the delivery system), is packaged in a tray that is sealed into an inner sterile barrier pouch, which is then labeled and sealed into an outer protective pouch.
- Labeled pouches are packaged into a shelf box with flip-top lid and closure seal.
- Labeling complies with 21 CFR § 812.5 and includes the statement, “CAUTON: Investigational device. Limited by Federal law to investigational use.”

Open tray here

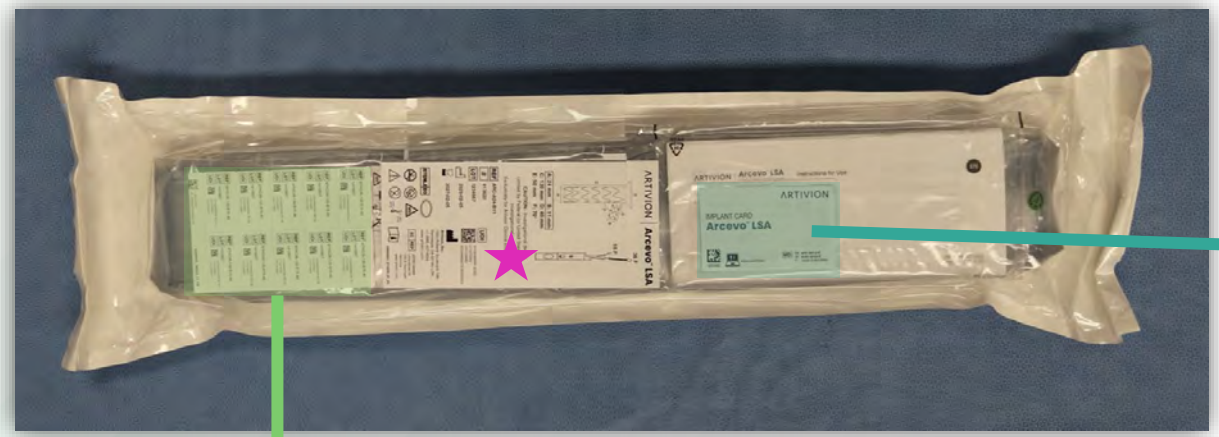
The IFU will be included within a document pouch attached to the device outer pouch.



Outer Pouch

The device's outer protective pouch has:

- Adhered document pouch with IFU
  - Adhered to IFU pouch is small clear sleeve which contains the implant card
- Adhered product label (pictured below with ★)
- 10 patient labels adhered directly to the outer pouch



The implant card is pictured below. Site staff need to write in the following information before providing to the patient:

1. Patient Identification: Patient name (first, middle, last) and/or patient ID
2. Date of implantation (YYYY-MM-DD)
3. Name and address of the implanting healthcare institution/provider and/or Physician's name

The **10** peel off **courtesy labels** are pictured above and example to the right. These labels are just for the site's purposes and do not need to be put on the implant card.

Device Removal from Packaging

Outside the sterile field:

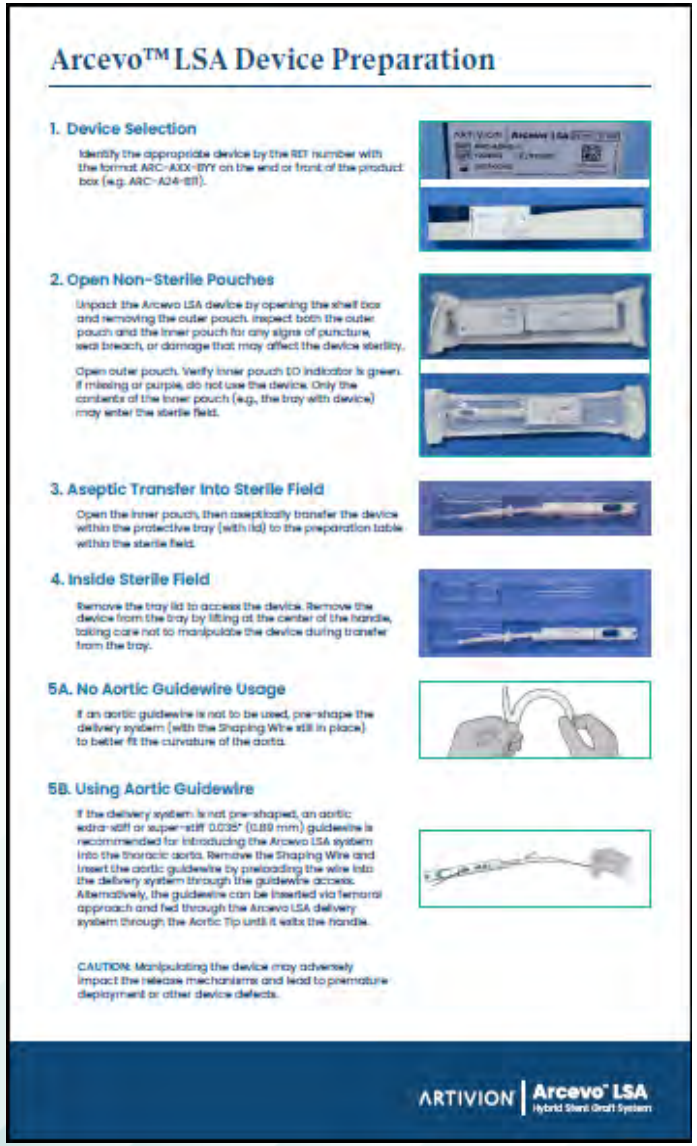
- Unpack the Arcevo LSA device by opening the shelf box and removing the outer pouch.
- Open the outer pouch to expose the inner pouch.
- Inspect all pouches for damage and do not use the device if grossly damaged or if device appears displaced or damaged within its protective tray.
- Only the contents of the inner pouch may enter the sterile field.
- Verify inner pouch contains a green EO indicator label to confirm product was sterilized. If missing or purple, do not use device.
- Open the inner pouch, then aseptically transfer the device within the protective tray to the sterile field.

Inside the sterile field:

- Once inside the sterile field, remove the tray lid to access the device.
- Remove the loaded Arcevo LSA device by lifting at the center of the handle, taking care not to manipulate the device during transfer from the tray.

Arcevo™ LSA Device Preparation

Each site will be provided digital and physical copies of the device sizing sheet pictured in the images below. Please make these accessible to all implanting investigators.



Arcevo™ LSA Device Preparation

1. Device Selection

Identify the appropriate device by the REF number with the format ARC-AXX-BYY on the end or front of the product box (e.g. ARC-A24-B11).

2. Open Non-Sterile Pouches

Unpack the Arcevo LSA device by opening the shelf box and removing the outer pouch. Inspect both the outer pouch and the inner pouch for any signs of puncture, seal breach, or damage that may affect the device sterility.

Open outer pouch. Verify inner pouch ED indicator is green. If missing or purple, do not use the device. Only the contents of the inner pouch (e.g., the tray with device) may enter the sterile field.

3. Aseptic Transfer Into Sterile Field

Open the inner pouch, then aseptically transfer the device within the protective tray (with lid) to the preparation table within the sterile field.

4. Inside Sterile Field

Remove the tray lid to access the device. Remove the device from the tray by lifting at the center of the handle, taking care not to manipulate the device during transfer from the tray.

5A. No Aortic Guidewire Usage

If an aortic guidewire is not to be used, pre-shape the delivery system (with the Shaping Wire still in place) to better fit the curvature of the aorta.

5B. Using Aortic Guidewire

If the delivery system is not pre-shaped, an aortic extra-stiff or super-stiff 0.035" (0.89 mm) guidewire is recommended for introducing the Arcevo LSA system into the thoracic aorta. Remove the Shaping Wire and insert the aortic guidewire by preloading the wire into the delivery system through the guidewire access. Alternatively, the guidewire can be inserted via femoral approach and fed through the Arcevo LSA delivery system through the Aortic Tip until it exits the handle.

CAUTION: Manipulating the device may adversely impact the release mechanisms and lead to premature deployment or other device defects.

ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

ARTIVION

Advancing Aortic Technologies with Purpose™

Scan the QR Codes to get quick access to essential Arcevo LSA™ resources

Arcevo LSA™ Deployment Guide

Arcevo™ LSA Animation

Caution: Investigational Device – Limited by the United States law to investigational use. Refer to the instructions for Use and other product insert documentation that accompanies each of these devices for indications, contraindications, warnings, precautions, possible complications, and instructions for use. All trademarks are owned by Artivion, Inc. or its subsidiaries. © 2025 Artivion, Inc. All rights reserved.

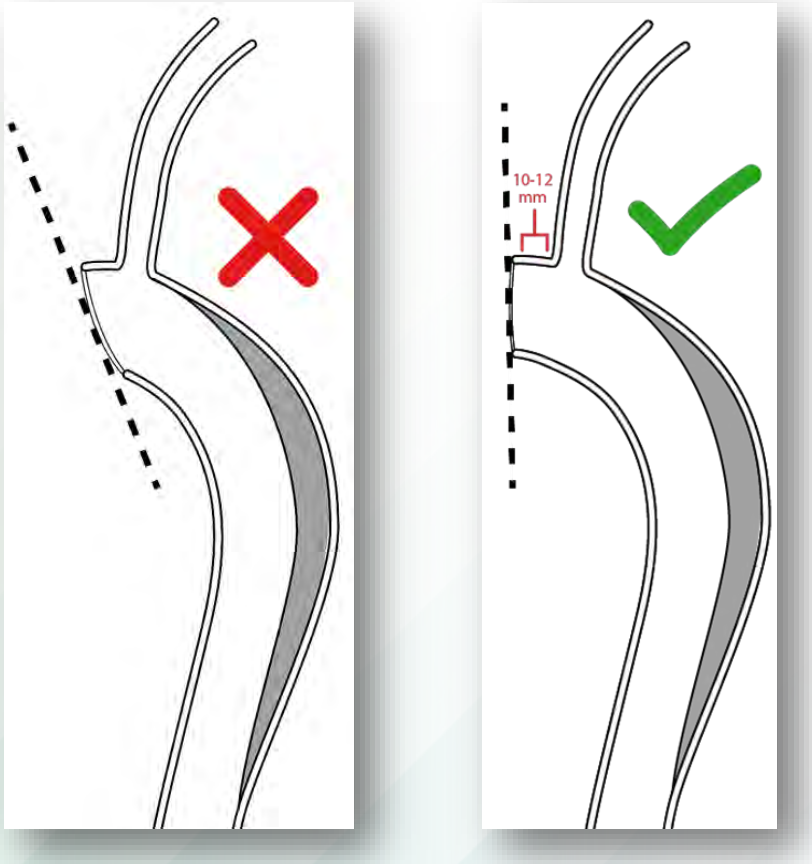
Artivion, Inc.
1655 Roberts Blvd. NW, Kennesaw, GA 30144 USA
Phone: 888-427-9654 | Fax: 770-590-3573 | E-mail: inquiries@artivion.com
For contact information by region, please visit: www.artivion.com/contact

Artivion, Inc., 1655 Roberts Blvd. NW, Kennesaw, GA 30144 USA

MLEN01928.000 (2025-08)

Deployment Steps

Arcevo LSA – Deployment Step 1

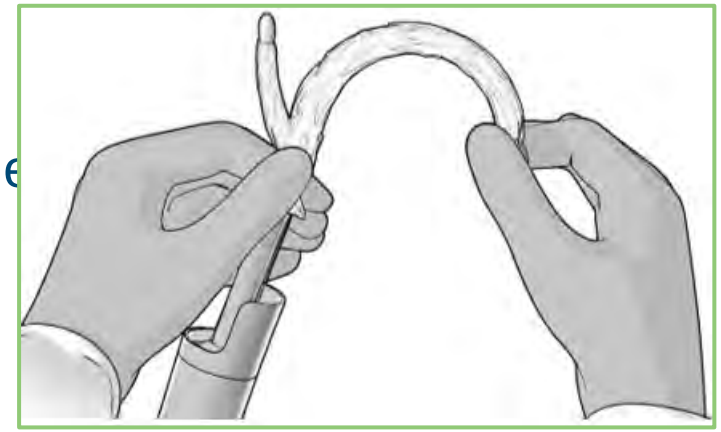


Transect the aorta perpendicularly in zone 2 by leaving at least 10 mm of aortic tissue proximal to the LSA.

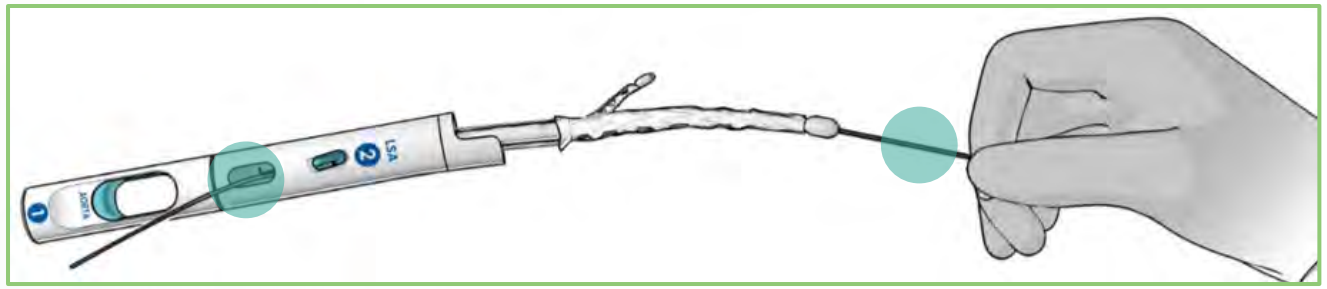
Guidewire Insertion – Deployment Steps 2 & 3

- Once Arcevo LSA has been removed from its packaging, the device preparation can begin.

No aortic guidewire used: Pre-shape the delivery system, with the Shaping Wire still in place, to approximate the aortic curvature.



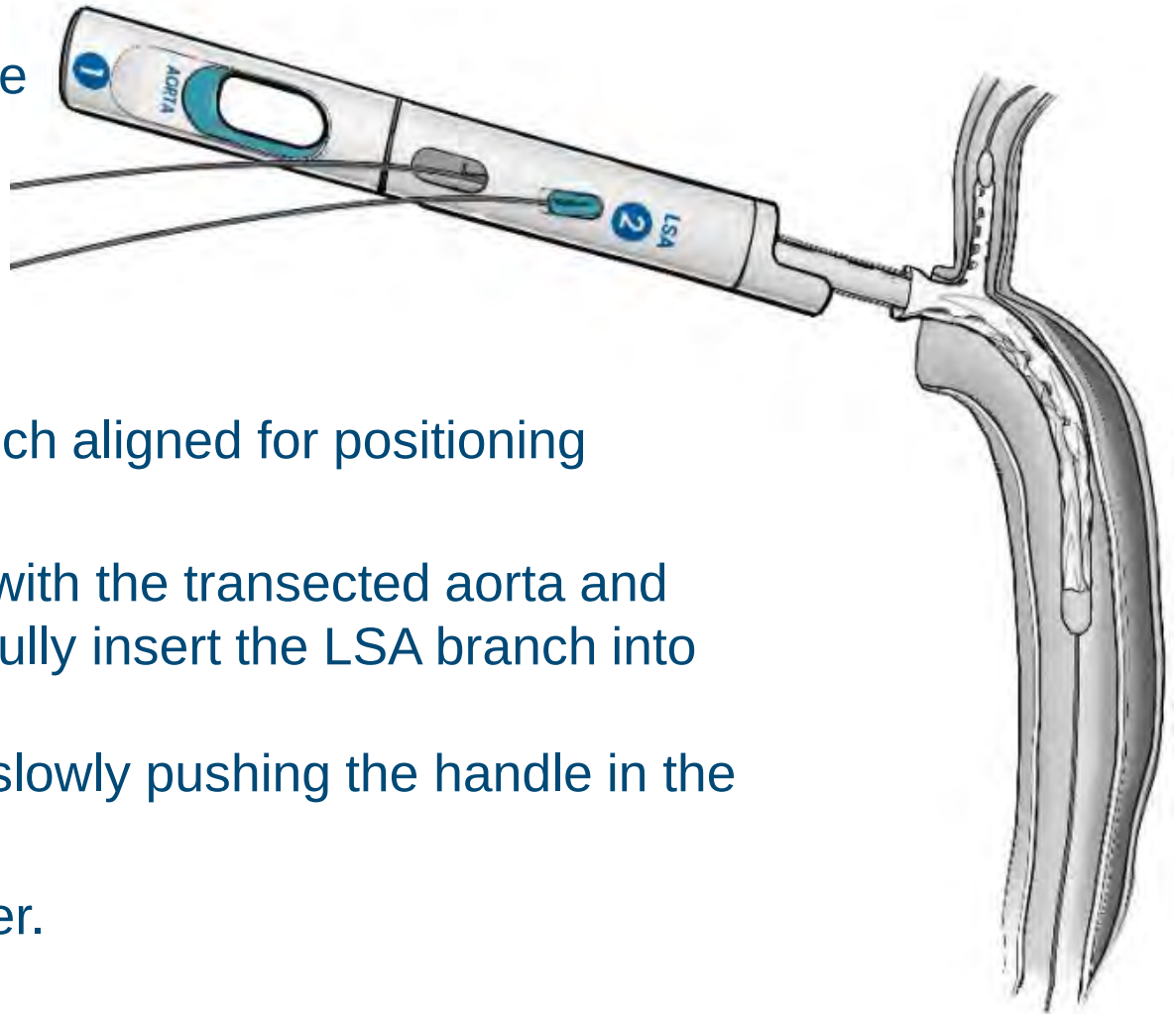
Using aortic guidewire: Remove the Shaping Wire and insert a 0.035” guide through the aortic tip, using antegrade or retrograde (femoral) approach.



- It is <u>strongly recommended</u> that a guidewire be used for insertion into the LSA.
- Insert the soft-tip 0.035” guidewire through the LSA guidewire lumen located at the base of the LSA tab until it exits the LSA Tip.

Inserting Arcevo LSA into Native Aorta – Deployment Step 4

- Align the Arcevo LSA branch with the location of the LSA vessel and advance the device into the transected aorta and LSA vessel, respectively.
- The Arcevo LSA delivery system should not be rotated once inserted into the aorta.



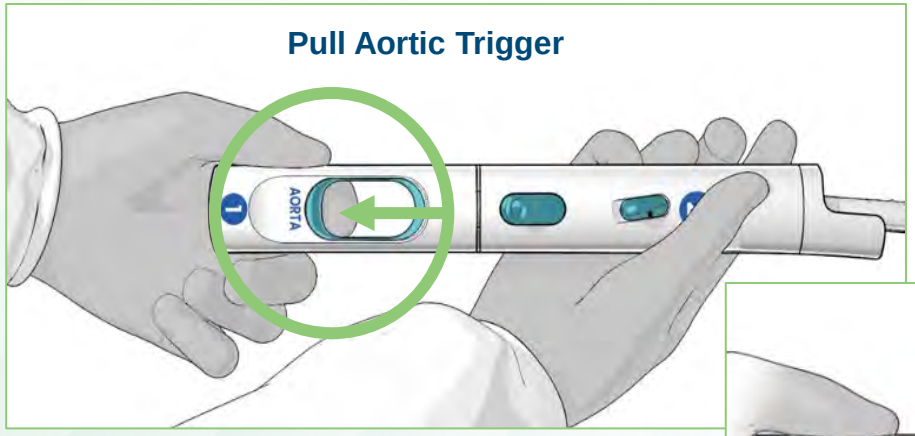
- Advance the Arcevo LSA device (with the LSA branch aligned for positioning into the LSA) into the transected aorta.
- Advance the delivery system until the collar aligns with the transected aorta and slowly push the handle to the outer aortic curve to fully insert the LSA branch into the LSA vessel.
- Fully insert the LSA branch into the LSA vessel by slowly pushing the handle in the direction of the outer curve.
- If excessive resistance is felt, do not advance further.

Aortic Stent Graft – Deployment Step 5

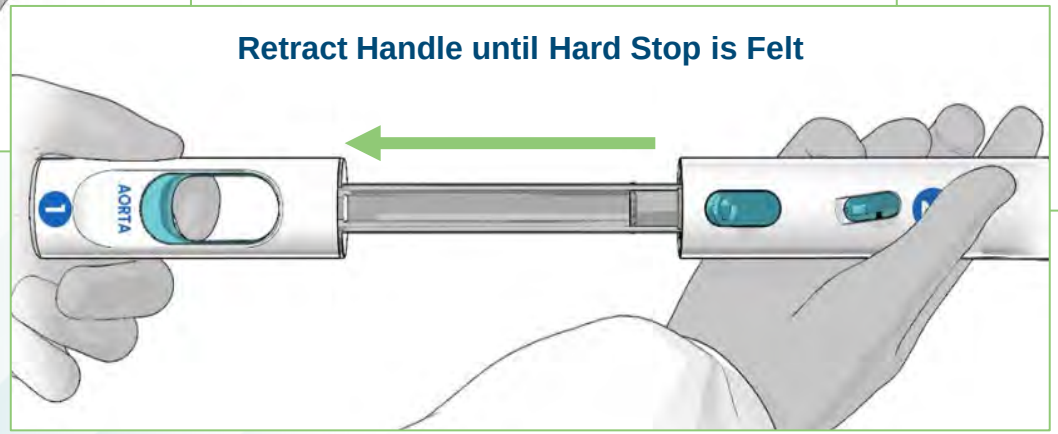
- While holding the handle steady to maintain position, deploy the aortic stent graft by pulling the trigger and retracting the handle until the delivery system locks.

TIP: Secure the implant by gently holding the device and aortic wall in place at the transection.

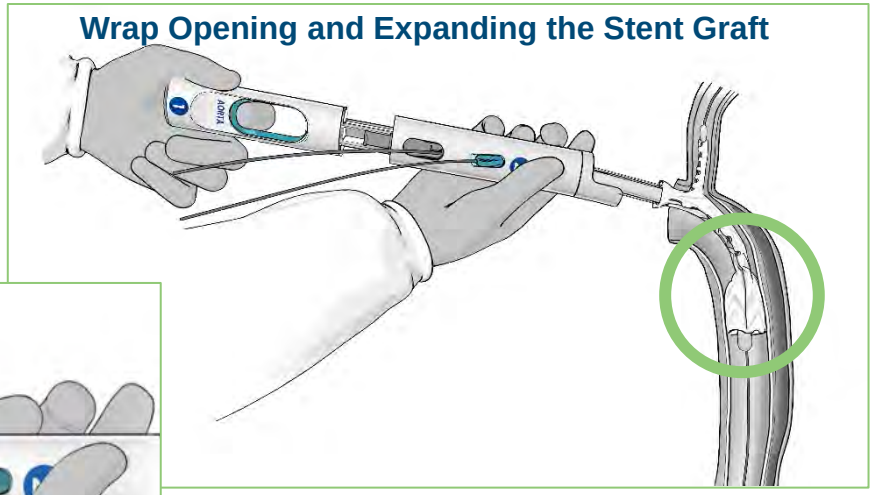
Pull Aortic Trigger



Retract Handle until Hard Stop is Felt



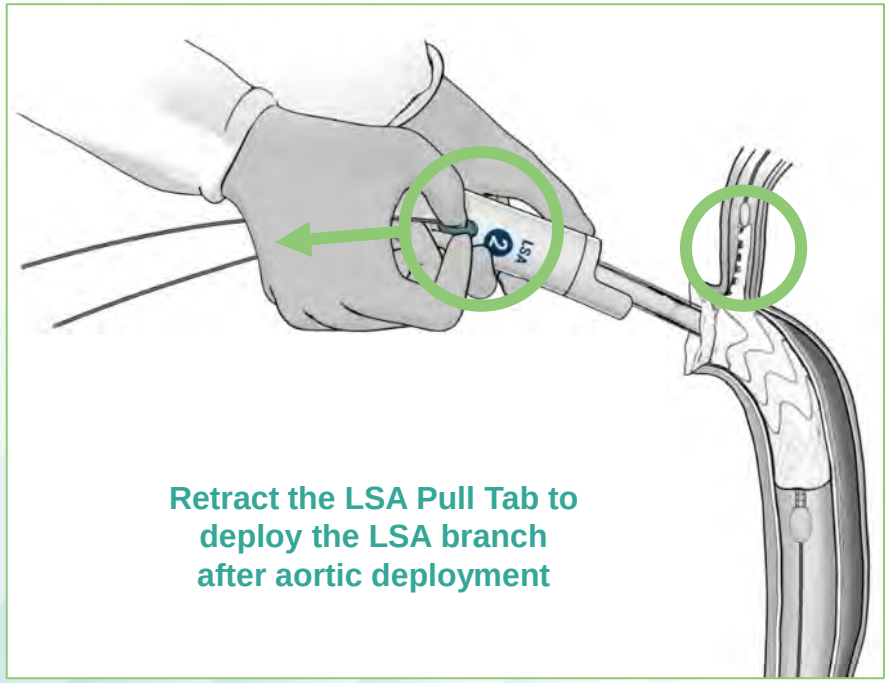
Wrap Opening and Expanding the Stent Graft



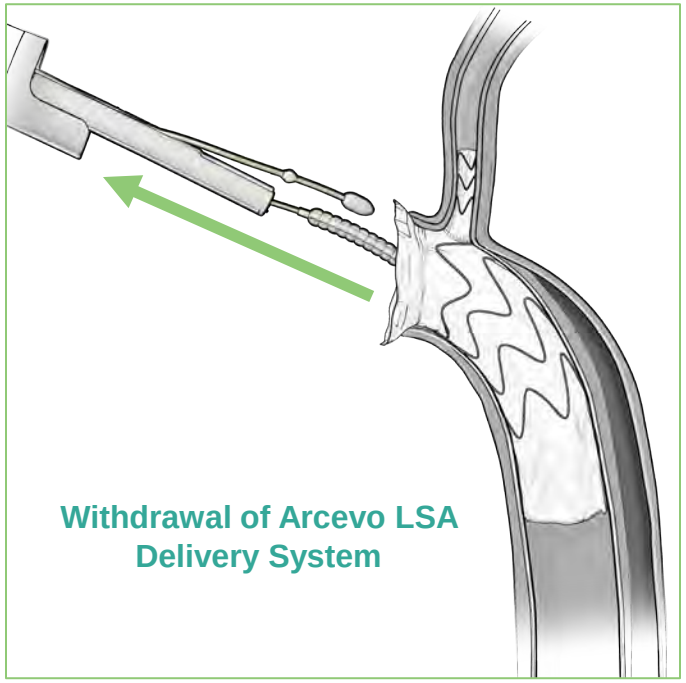
ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

LSA Branch & Delivery System Removal – Deployment Steps 6 & 7

- Pull the LSA Pull Tab to unlace the LSA Wrap and expand the LSA stented branch.
- Continue to retract the LSA Deployment Wire via the LSA Pull Tab until resistance is felt and the LSA Tip retracts toward the handle.
- Remove the Shaping Wire and/or any guidewires. Carefully withdraw the delivery system using slight rotational movements, if needed.

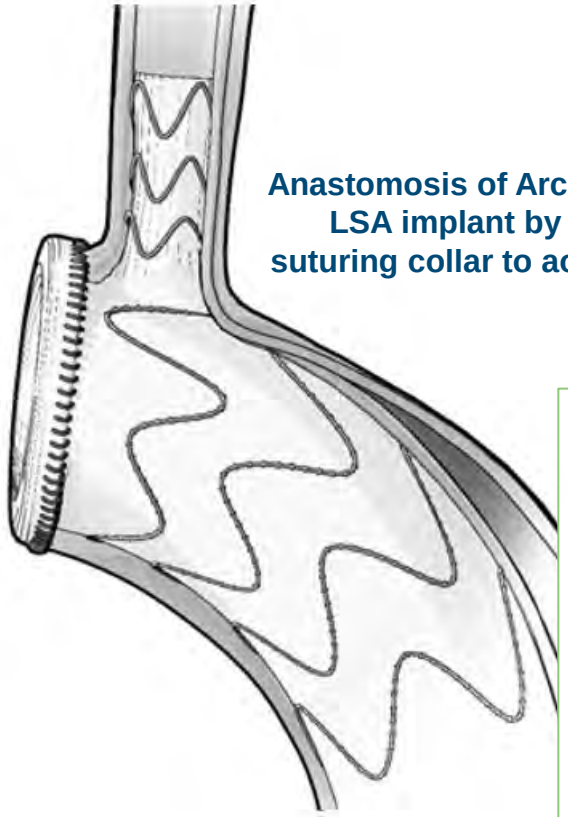


Retract the LSA Pull Tab to deploy the LSA branch after aortic deployment



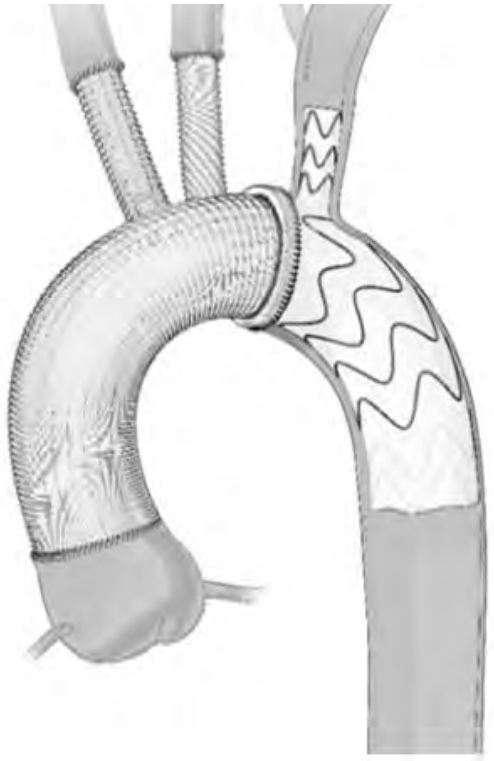
Withdrawal of Arcevo LSA Delivery System

Arcevo LSA Surgical Graft Anastomoses – Deployment Step 8



Anastomosis of Arcevo LSA implant by suturing collar to aorta

Representative Total Arch Replacement with Arcevo LSA Implant



- **First Anastomosis**
  Anastomose the Arcevo LSA collar to the transected aorta using standard surgical techniques.
- **Second Anastomosis**
  Perform the desired arch repair with the surgical graft of choice using institutional protocol. Anastomose the surgical graft to the Arcevo LSA/Aorta construct at Zone 2 using standard surgical techniques.

TEVAR – Deployment Step 9 (Optional)

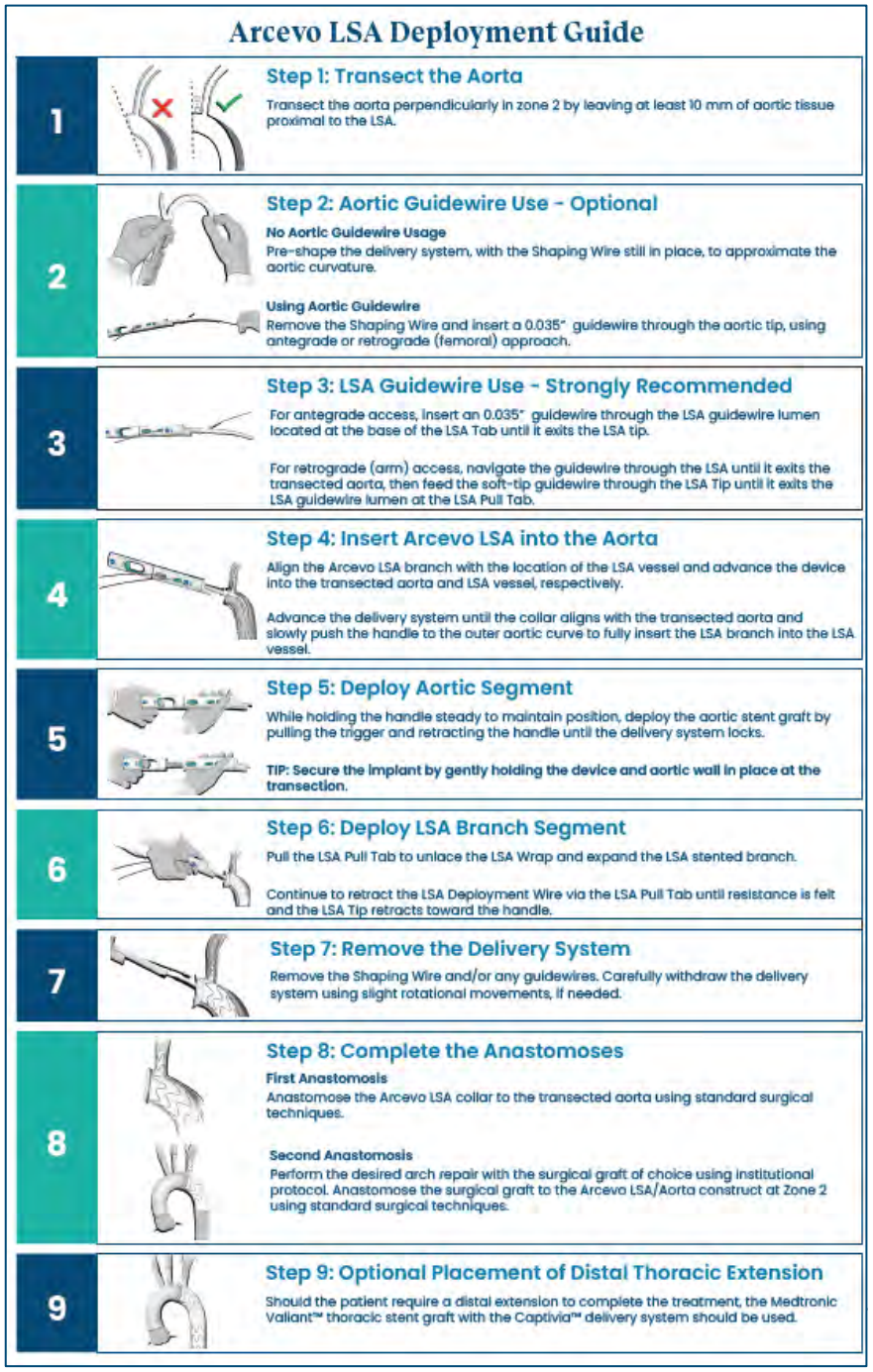
Distal Placement of Endovascular Thoracic Extension

- Should the patient require a distal extension to complete the treatment, the Medtronic Valiant™ thoracic stent graft with the Captivia™ delivery system should be used.
    - Closed Web, straight or tapered, 24-44 mm may be used with Arcevo LSA.
    - Implantation of the Medtronic Valiant™ thoracic stent graft is to be performed in accordance with the manufacturer's IFU.
    - Take care to manage the Arcevo LSA implant during insertion and positioning to not displace the stent or cover the LSA.
    - Confirm position and alignment via fluoroscopy.

Arcevo LSA Deployment Animation

Deployment Guide

Each site will be provided digital and physical copies of the Deployment Guide pictured in the image to the right. Please make these accessible to all implanting investigators.



Arcevo LSA Deployment Guide

1

Step 1: Transect the Aorta

Transect the aorta perpendicularly in zone 2 by leaving at least 10 mm of aortic tissue proximal to the LSA.

2

Step 2: Aortic Guidewire Use - Optional

No Aortic Guidewire Usage

Pre-shape the delivery system, with the Shaping Wire still in place, to approximate the aortic curvature.

Using Aortic Guidewire

Remove the Shaping Wire and insert a 0.035" guidewire through the aortic tip, using antegrade or retrograde (femoral) approach.

3

Step 3: LSA Guidewire Use - Strongly Recommended

For antegrade access, insert an 0.035" guidewire through the LSA guidewire lumen located at the base of the LSA Tab until it exits the LSA tip.

For retrograde (arm) access, navigate the guidewire through the LSA until it exits the transected aorta, then feed the soft-tip guidewire through the LSA Tip until it exits the LSA guidewire lumen at the LSA Pull Tab.

4

Step 4: Insert Arcevo LSA into the Aorta

Align the Arcevo LSA branch with the location of the LSA vessel and advance the device into the transected aorta and LSA vessel, respectively.

Advance the delivery system until the collar aligns with the transected aorta and slowly push the handle to the outer aortic curve to fully insert the LSA branch into the LSA vessel.

5

Step 5: Deploy Aortic Segment

While holding the handle steady to maintain position, deploy the aortic stent graft by pulling the trigger and retracting the handle until the delivery system locks.

TIP: Secure the implant by gently holding the device and aortic wall in place at the transection.

6

Step 6: Deploy LSA Branch Segment

Pull the LSA Pull Tab to unlace the LSA Wrap and expand the LSA stented branch.

Continue to retract the LSA Deployment Wire via the LSA Pull Tab until resistance is felt and the LSA Tip retracts toward the handle.

7

Step 7: Remove the Delivery System

Remove the Shaping Wire and/or any guidewires. Carefully withdraw the delivery system using slight rotational movements, if needed.

8

Step 8: Complete the Anastomoses

First Anastomosis

Anastomose the Arcevo LSA collar to the transected aorta using standard surgical techniques.

Second Anastomosis

Perform the desired arch repair with the surgical graft of choice using institutional protocol. Anastomose the surgical graft to the Arcevo LSA/Aorta construct at Zone 2 using standard surgical techniques.

9

Step 9: Optional Placement of Distal Thoracic Extension

Should the patient require a distal extension to complete the treatment, the Medtronic Valiant™ thoracic stent graft with the Captivia™ delivery system should be used.

Case Review Process

Requirements and Materials for Implanting Surgeons

- The PI and any sub-investigator *who will be implanting Arcevo LSA (i.e., a cardiac surgeon)* must have a demonstrated history of **independently** implanting **≥5** total arch replacement (TAR) procedures **in the last year** to be activated on the study
  - The PI will be responsible for confirming that their sub-investigators meet this requirement
  - Vascular surgeons can still be a sub-investigator and this requirement wouldn't be applicable since they will not be implanting Arcevo LSA
  - Other requests for non-implanting sub-investigators should be submitted to an Artivion PM
- Device training will include both review of this SIV training presentation, as well as an opportunity for hands on deployment of Arcevo LSA within a model
- Implanting investigators will be provided with a 1-page, double sided deployment quick reference guide for the Arcevo LSA procedure and a 1-page double sided sizing sheet for case planning purposes

Case Review

- Case reviews are scheduled between an Artivion Therapy Development Manager and the implanting surgeon to review case details, including the CTA
- The purpose of the case review is to (1) confirm patient eligibility for the study, (2) ensure correct device size selection, and (3) provide opportunity to answer surgeon's questions
- The following are case review requirements:
  - Case review **is required for each site's first 2 enrolled cases** (which are required to be elective); case review is *optional* after that; the cases may be treated by the same implanting surgeon or 2 different surgeons
  - Review will occur after a patient is consented and before the patient's surgery
  - Case reviews will likely take <30 mins and occur remotely
  - CTA review is required to confirm anatomical eligibility criteria; review can occur via screenshare or FaceTime
- Additional case review is optional beyond the site's first 2 enrolled cases; the site would reach out to their therapy manager to schedule any requested review
- The Investigator and study staff remain responsible for medically screening all patients

Case Support

Case Support

- Case support includes in-person and virtual support by an Artivion Therapy Manager; 24-hr virtual support is offered
- Support will include answering questions about Arcevo LSA implantation, device sizing, and patient eligibility
- In-person case support is **required for each site's first case**
- Case support after each site's first case is optional; the site would reach out to the Therapy Manager to request any additional case support
- Contact information for the Artivion Therapy Manager is:

  Name: Don Jolley
  Title: Senior Manager – Therapy Development
  Cell Phone: 440-821-2131
  E-mail Address: Don.Jolley@artivion.com
  Home Base: Ohio (ET)

- All implanting investigators should save Don's contact information in their cell phones

Investigators:
Hands-on Device Training and Deployments

Site Staff:
Site Team Breakout

Site Team Breakout:
Protocol Deviations

Protocol Deviations

- Any non-adherence to or divergence from the protocol-specific study procedures
- Protocol deviations include *unplanned* incidences of protocol non-compliance
- **Site Responsibilities**:
  - Identify deviations and report to the IRB of record (per their requirements)
  - Enter required information about all deviations into the Protocol Deviation eCRF
  - PI to assess severity of each deviation per IRB guidance
- A protocol deviation undertaken to eliminate an apparent immediate hazard to patients or to protect the life or physical wellbeing of the patient in an emergency is a special circumstance that must be reported to the sponsor and the reviewing IRB/EC within 5 working days
  - These emergency deviations must be documented and are subject to retrospective review
  - No other type of prospective protocol deviation is permitted without prior approval
- Deviations will be monitored and reviewed by CRAs and escalated to PMs, as needed
- Repeated deviations will be evaluated and may require a corrective action plan, further training, additional monitoring, suspension of activities, and/or further action from the sponsor

Protocol Deviations (cont.)

- Data entry into the Protocol Deviation eCRF includes the following:
  - Date of when deviation occurred
  - Date when reported to Sponsor (i.e., date of data entry into eCRF)
  - Associated visit (as applicable)
  - Deviation Type (w/ preset list of most common deviations)
    - Please review the list thoroughly before selecting the type that most accurately captures the deviation
    - If Other issue is selected, please provide a succinct description
  - Severity assessment, including:
    - Date of assessment
    - Name of assessor
    - Reportability to overseeing IRB
    - If applicable, date of reporting to IRB

Important Protocol Deviations:

- An **important protocol** deviation is a subset of protocol deviations that might significantly affect the completeness, accuracy, and/or reliability of the study data or that might significantly affect a subject's rights, safety, or well-being.
  - The term 'important' aligns with FDA's Guidance Document titled "*Protocol Deviations for Clinical Investigations of Drugs, Biological Products, and Devices*"
  - Important is essentially the same as major or significant
- Examples of important protocol deviations include:
  - Failure to obtain informed consent is defined as:
    - an ICF not signed by a required party,
    - consent not obtained prior to study specific procedures being performed, or
    - consent obtained by non-delegated or non-trained personnel
  - Enrollment of a subject who does not meet eligibility criteria
  - Failure to protect the subject's identifiable private protected health information (PHI)
  - Failure to conduct study procedures designed to protect or assess participant safety
  - Failure to complete diagnostic imaging without due cause

Important Protocol Deviations (cont.):

- Examples of important protocol deviations include:
  - Failure to administer the study product according to this protocol, associated plan, or the IFU
  - Use of expired product
  - Use of a TEVAR device that is not the Valiant™ Captivia™
  - Failure to collect data to evaluate the primary safety and effectiveness endpoint through 1-year follow-up

Escalation of Protocol Deviations

- Artivion CRAs and PMs hold regular site management meetings to review site protocol deviations and other metrics
- The following may occur for repeated deviations:
  - Increase in monitoring frequency, at a minimum
  - ≥2 important deviations (not related to preservation of life/health) can result in suspension of enrollment at the site
  - ≥3 repeated minor deviations will result in escalation to site PI and site research compliance staff
  - If required, Site PM and CRA will may ask site staff to develop a corrective action plan to prevent further deviations (which may result in your site issuing a CAPA).
    - Corrective actions may include retraining, increased IMVs, updated procedures/processes, internal site audits etc.
    - Compliance with site action plans will be assessed at each IMV
- Escalation actions will be documented in the monitoring letter and/or follow-up letter, with the applicable deviation information.

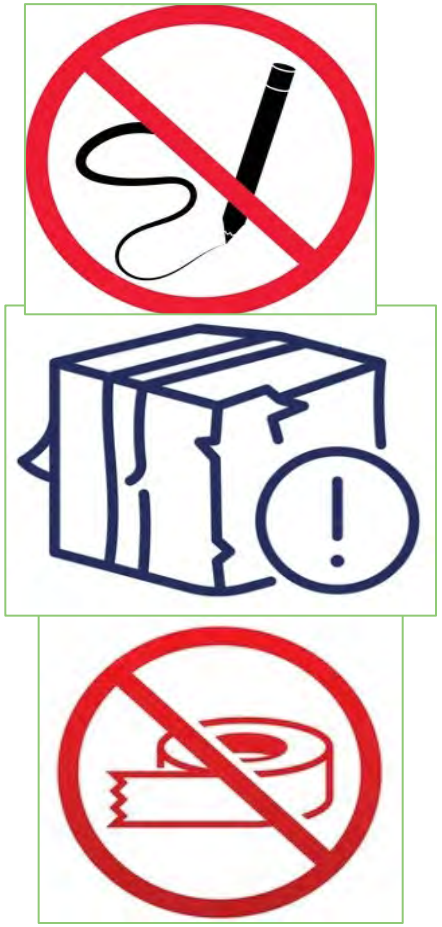
Site Team Breakout:
Device Storage

Device Storage

- Each site will be responsible for storing *a minimum* of 7 Arcevo LSA boxes at a time at each approved site location
  - Box Dimensions: 2.6” x 3.9” x 24.5”
- The site may receive additional devices if a special device size is ordered that is not part of the ‘starter pack’
- The devices must be stored at room temperature (between 5°C and 25°C [41°F to 77°F])
  - Room / storage area temperatures will not be logged, however the site will be asked to confirm the temperature range of the area and monitors will check during IMVs
- The devices must be stored in a secure location and not with other commercial devices
- The devices must only be available to implanting surgeons who have been activated on the study
- The devices must be easily available in the event of an emergent case

Device Handling

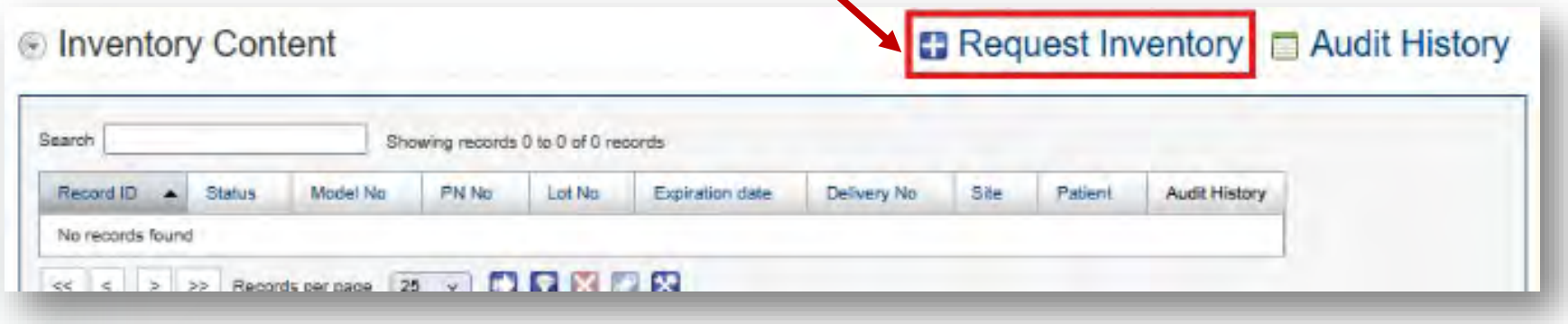
- For any Arcevo LSA devices received at the site, sites are NOT to:
  - Mark-up or write on the box in any way
  - Damage the box or store in a way that dents the box
  - Put tape, stickers, or other adhesives on the box
  - Open the box without intension of use
- If a device needs to be returned for any reason, it should be in the same condition returned as it was when it was delivered
  - Artivion may be able to use device for a different case/site
- Boxes that are opened, but not used, must be returned to Artivion (**NOT** thrown out)



Site Team Breakout:
Product Ordering and Billing

Device Orders and Receipt

- Prior to site activation, each study site location will receive 7 devices on consignment, and these are referred to as the “starter-pack”.
- ARTIZEN PM will need shipping address and contact info for study personnel responsible for receipt prior to shipment.
- A starter-pack includes 1 each of the following sizes (list by product code):
  - ARC-A28-B11, ARC-A28-B15, ARC-A30-B11, ARC-A30-B15, ARC-A33-B11, ARC-A33-B15, ARC-A36-B15
- If a patient is consented and meets the criteria for a device that isn’t in the starter-pack, the site can place an order by e-mailing their assigned ARTIZEN PM or through the EDC; the other 4 sizes include: ARC-A24-B11, ARC-A26-B11, ARC-A36-B11, ARC-A40-B15



- **Devices currently have a 6-month shelf life and are due to expire between Jan and Feb 2026.**
- **If you received these devices, we will ask for them to be returned prior to expiration and you will receive replacement devices.**

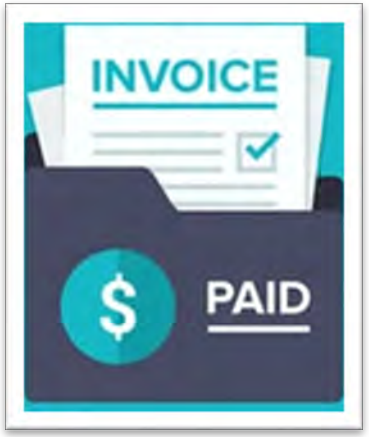
Device Orders and Receipt (cont.)

- If required by the site, sites should provide a no-charge PO # for all orders and that number will be included on the exterior of the box; any delays in providing the PO # will result in a delay in shipment
- Study site documents receipt of all IP in the Inventory Module of the EDC
  - Device details will be pre-populated by the CRO (including lot numbers), but site data entry, including confirmation of receipt will be required
  - Site is to verify contents and inspect for damage
    - If device and/or box is damaged or in case of a content discrepancy, contact your Artivion PM or study team at ARTIZEN@artivion.com
- The Valiant Captivia device is ordered through Medtronic, which can be facilitated by your local sales rep
  - Artivion is not involved in these orders; the assumption is you have access to the devices and make the correct size available prior to the scheduled procedure

Device Return

- A study site could return an Arcevo LSA device for several reasons including but not limited to sponsor request, IP unused at end of enrollment, defective product, damaged device, expired device, or package opened and unused.
- The site will contact the study team at ARTIZEN@artivion.com or the Artivion PM with the following details for each device requiring return: model number and lot number.
- Artivion PM will provide the pre-printed shipping label to the site and the site will ship the device(s) back.
- The details on the device return will be updated in the inventory module by the CRO (Bright)
    - Any inconsistencies with information in the module should be communicated to your Artivion PM

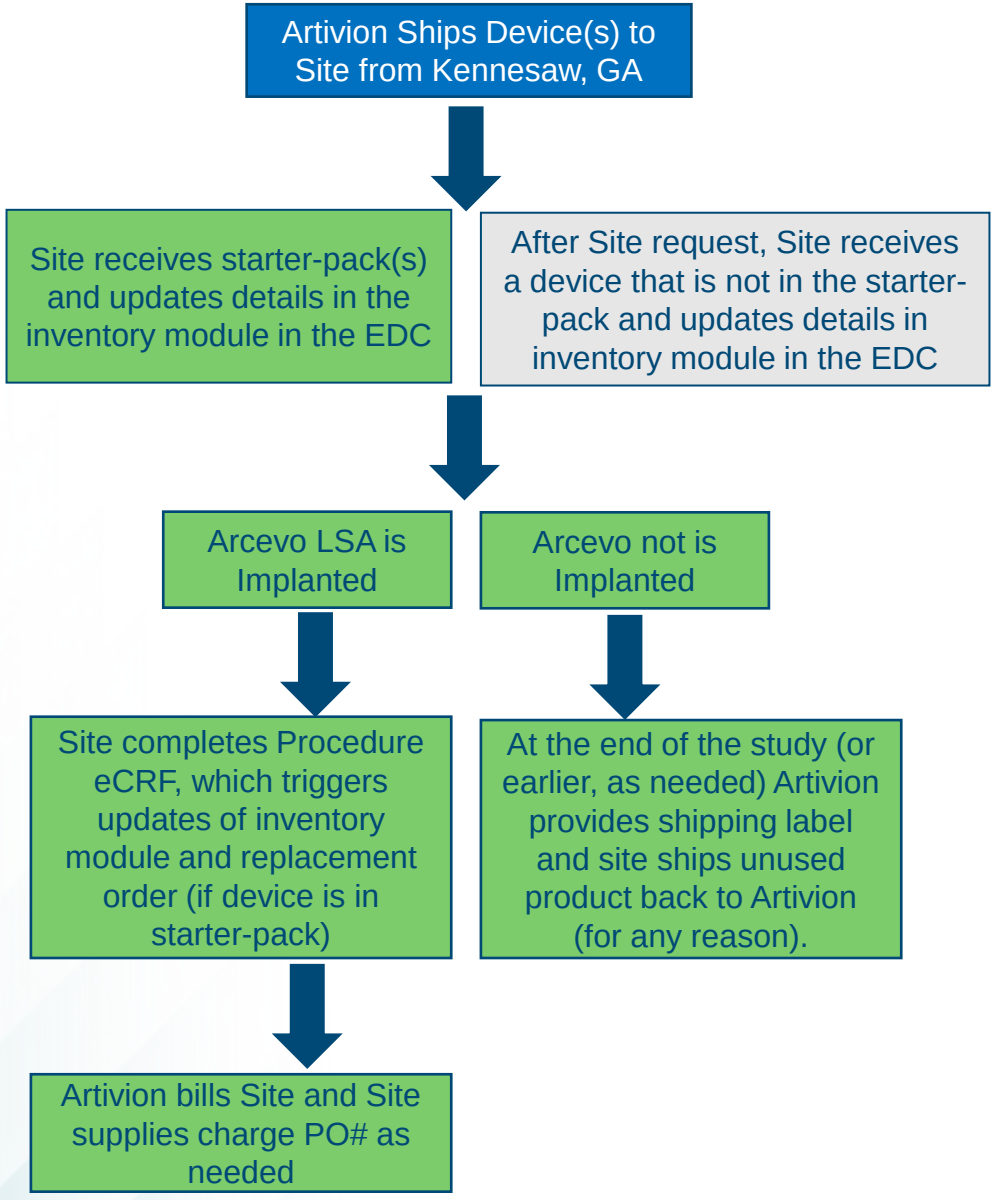
Device Billing and Replacement



- Once a device is implanted, the site should provide a charge PO # (if site required) and enter the applicable information in the Procedure eCRF
- The inventory module will automatically update with the information from the Procedure eCRF, so no additional work is required.
- ARTIZEN study team will notify Artivion customer service to initiate invoicing using the billing e-mail address provided by the site
- If the device used was a starter-pack size, the Artivion PM will initiate a replacement order and another no-charge PO # may be required (depending on the site)
    - Artivion will make all efforts to replace the device quickly, but this will be subject to device availability

18. How many Arcevo LSA devices are in the starter-pack that will be stored on-site?

ARTIZEN Study Investigational Product (IP) Flowchart



Confidential

Site Team Breakout:
Documenting Early Termination

Documenting Early Termination

Withdrawal:

- Participation is completely voluntary; the patient is free to withdraw from the study at any time.
- An Investigator may also withdraw the patient from the study in the event of illness, adverse events, or other reasons concerning the health or wellbeing of the patient, or in the case of lack of cooperation.
  - Should a patient or Investigator decide a withdrawal is needed, all efforts will be made to complete and report the observations up to the time of withdrawal.

Lost-to-Follow-up:

- Site can consider a patient lost-to-follow-up if they meet the following criteria:
  - Failure to complete 2 consecutive follow-up visits (without due cause) AND
  - Documentation of 3 unsuccessful attempts by the research staff to contact the patient or next of kin, including at least one letter sent by certified mail.
- Final evaluation of the patient will be the last clinic visit for which the patient was present

Adverse Event (including death or Arcevo LSA explant):

- If the reason for the withdrawal is a clinical adverse event (fatal or not fatal), it must be recorded in the **Adverse Event eCRF**
- If the reason for withdrawal is Arcevo LSA explant, it must be recorded in the **Additional Post-Operative Procedure eCRF**

Sites must complete the **Study Exit eCRF** for all of the reasons listed above

Lunch

Core Lab

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Cleveland Clinic Imaging Core Lab – Project Team

Francis Caputo, MD

Core Lab Study PI

Sara McDaniel, Brett Babb, Tom Fultz, Paul Bishop, and Lindsay Feiten

Core Lab – Overview

- Vascular Core Lab is a research only group separate from Clinical Operations at Cleveland Clinic
- Vascular Core Lab has been assessing medical imaging for clinical trials for 30+ years!
- Core Lab will be collecting medical imaging from all sites
  - Provide a detailed qualitative and quantitative diagnostic image analysis for all required imaging
  - Identify and/or investigate all instances of suspected device integrity issues
- Core Lab is performing a uniform analysis on all submitted images
  - 80+ Analysis Data points
  - Full Device Integrity Analysis
- Core Lab Results reported directly to Artivion
  - Sites will be sent significant findings from an Artivion PM and asked to confirm if the finding has any clinical impact

Core Lab Responsibilities

- Train sites on diagnostic imaging recommendations and use of program for uploading imaging files (AGMednet)
- Provide a detailed qualitative and quantitative diagnostic image analysis for all required imaging
- Identify and/or investigate all instances of suspected device integrity issues
- Communicate and document Significant Findings
    - o Sites will be sent significant findings from the Core Lab, via the Artivion Project Manager, and asked to confirm if the finding has any clinical impact
- Serve as subject matter expert

Core Lab – Contact Information

- Email: corelab@ccf.org (**Please email for fastest response*)
- Phone: 216-444-8880
- Mailing Address:

  Cleveland Clinic Vascular Core Lab

  9500 Euclid Ave, JJ65

  Cleveland Ohio, 44195

Image Submission Process

Imaging Protocol

- Imaging of chest, abdomen, and (preferably) pelvis will be collected pre-op and at all follow-up visits
- Imaging should include visualization of the following:
  - Ascending aorta
  - Aortic arch
  - Supra-aortic vessels, including carotid bifurcation and cervical portion of the internal carotid artery and vertebral arteries
  - Descending aorta
  - Abdominal aorta
  - Aortic bifurcation (ideally)
- Computed tomography angiography (CTA) is preferred
  - Three phase CT (non-contrast, contrast, and delayed phase)
- Preferred slice spacing: 0.65 mm to 3 mm (thinner preferred)
- Imaging is performed locally and submitted to CCF Core Lab via AGMedNet
  - All patient imaging **must be de-identified prior** to uploading to AGMedNet
  - All questions pertaining to the upload of imaging must be directed to AGMedNet IT support
- **Sites** will enter the **visit information** in the **Imaging eCRF** and the Core Lab staff will complete the remainder of the Imaging eCRFs.
  - Sites will have read only access to the Core Lab entered data

Electronic Submission of Imaging

AGMEDNET Portal for Electronic Imaging Submission:

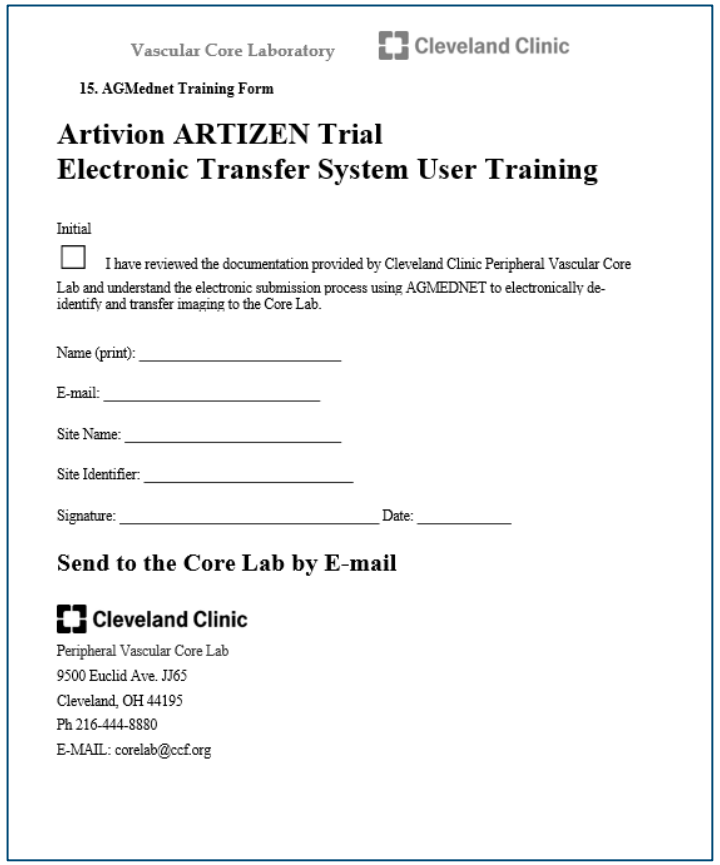
- 21CFR Part 11 Compliant
- De-identifies DICOM headers prior to imaging leaving site
  - ***Always de-identify imaging using site methods before uploading***
- Secure transfer of imaging to Core Lab
  - AES-256 Encryption
- Core Lab will receive imaging typically within minutes of sending
- All Transfers are tracked and logged

AGMEDNET imaging submission process will be familiar if you have used it for other trials!

Obtaining Access to Electronic Transfer System

- Review provided AGMEDNET Training
- Return Training form to Core Lab via email
- Core Lab will grant access

AGMEDNET Self-Training Guide



Vascular Core Laboratory Cleveland Clinic

15. AGMednet Training Form

Artivion ARTIZEN Trial
Electronic Transfer System User Training

Initial

☐ I have reviewed the documentation provided by Cleveland Clinic Peripheral Vascular Core Lab and understand the electronic submission process using AGMEDNET to electronically de-identify and transfer imaging to the Core Lab.

Name (print): _____

E-mail: _____

Site Name: _____

Site Identifier: _____

Signature: _____ Date: _____

Send to the Core Lab by E-mail

Cleveland Clinic
Peripheral Vascular Core Lab
9500 Euclid Ave. JJ65
Cleveland, OH 44195
Ph 216-444-8880
E-MAIL: corelab@ccf.org

AGMEDNET Self-Training Form

AG Mednet Support

- Helpdesk available 24 hours a day, 7 days a week, 365 days a year
  - Phone: +1-888-9-AGMEDNET (888-924-6336)
  - Email: support@agmednet.com (Response within 1 business Day)

- Contact the Core Lab if you are unable to solve transfer issues with AG Mednet support.

Common Imaging Issues

- Imaging containing PHI uploaded to Core Lab
  - The following information is not required as part of image submission and are a common place to find PHI:
    - Dose reports
    - Order forms
    - Screen captures
- Imaging Transfer Issues – entire scan doesn't fully upload
- Non-Contrast only imaging
- Imaging doesn't include the full or correct anatomy

- TIP: If there is a known compliance issue with the imaging you're submitting to the Core Lab, please let the Core Lab know in the comments section to reduce the number of queries.

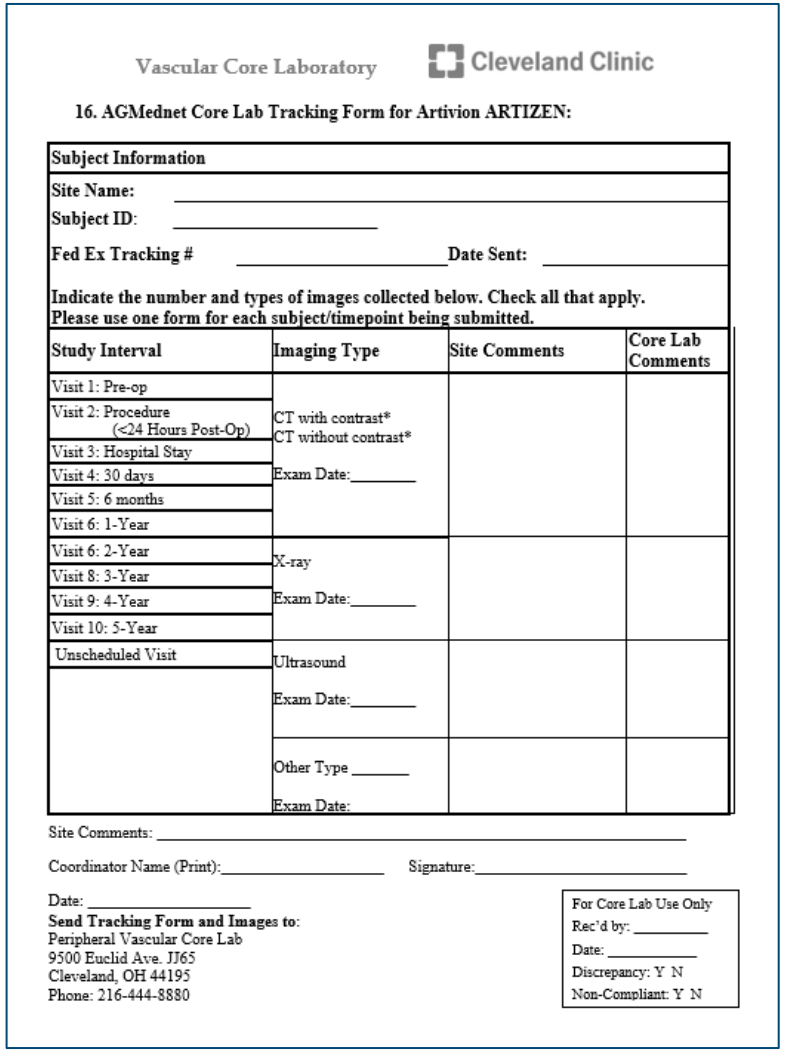
Image Submission Process – Mail In

Physical Shipment of Imaging to Core Lab

- Electronic Transfer is Preferred; however, the Core Lab can accept physical Shipments (if there is no other option)
- De-identify all imaging prior to shipment
- Utilize appropriate physical media for transfer
- Shipment must include “Core Lab Tracking Form” found in Site Manual
- Please be sure to correctly address shipment
  - Use sponsor provided shipping account
  - Address shipment using full Core Lab Mailing Address

Mailing Address for Physical Shipments:

Cleveland Clinic Vascular Core Lab
9500 Euclid Ave, JJ65
Cleveland Ohio, 44195



Vascular Core Laboratory — Cleveland Clinic

16. AGMednet Core Lab Tracking Form for Artivion ARTIZEN:

Subject Information

Site Name: _____

Subject ID: _____

Fed Ex Tracking # _____ **Date Sent:** _____

Indicate the number and types of images collected below. Check all that apply. Please use one form for each subject/timepoint being submitted.

Study Interval	Imaging Type	Site Comments	Core Lab Comments
Visit 1: Pre-op			
Visit 2: Procedure (<24 Hours Post-Op)	CT with contrast* CT without contrast*		
Visit 3: Hospital Stay			
Visit 4: 30 days	Exam Date:_____		
Visit 5: 6 months			
Visit 6: 1-Year			
Visit 6: 2-Year	X-ray		
Visit 8: 3-Year			
Visit 9: 4-Year	Exam Date:_____		
Visit 10: 5-Year			
Unscheduled Visit	Ultrasound		
	Exam Date:_____		
	Other Type _____		
	Exam Date:		

Site Comments: _____

Coordinator Name (Print):_____ Signature:_____

Date: _____

Send Tracking Form and Images to:
Peripheral Vascular Core Lab
9500 Euclid Ave. JJ65
Cleveland, OH 44195
Phone: 216-444-8880

For Core Lab Use Only
Rec’d by: _____
Date: _____
Discrepancy: Y N
Non-Compliant: Y N

Sample Core Lab Tracking Form

Recommended Imaging Protocol

CTA Scan Requirements

- Goal: Best quality imaging possible
- Guidelines provided for study are not meant to be restrictive.
- Wide variety of scanner configurations and site protocols anticipated.
- Sites should use their standard radiation reduction techniques

SCHEDULE OF IMAGING

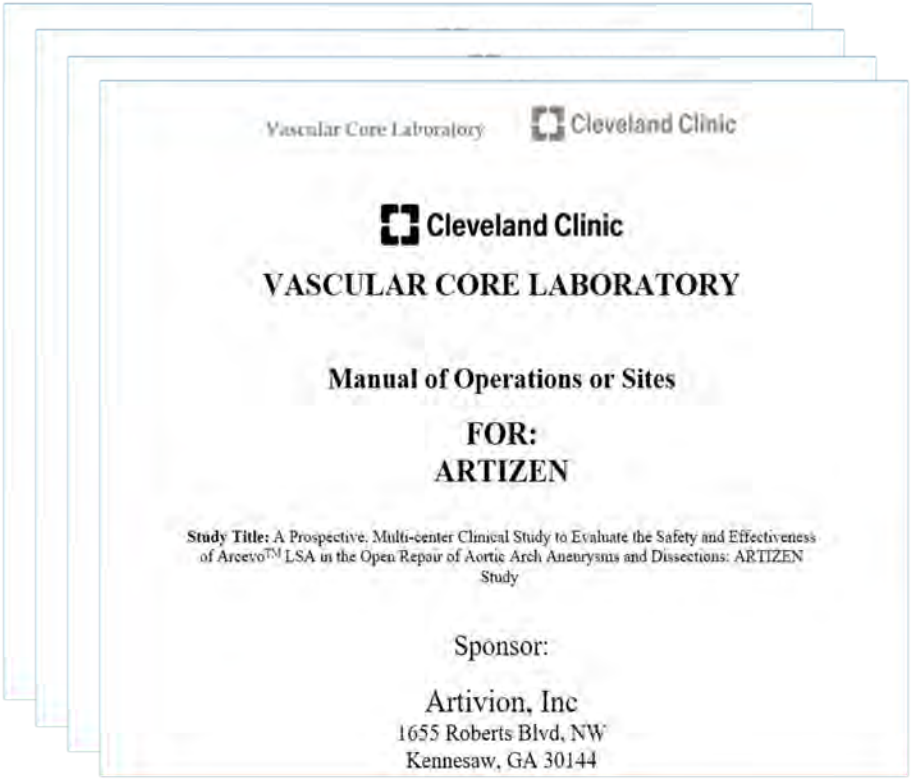
Procedures	Visit 1: Pre-Procedure	Visit 2: Procedure/ Discharge	Visit 3: Hospital Stay	Visit 4: 30-Days	Visit 5: 6-Months	Visits 6-10: 1, 2, 3, 4, 5 Years	Unscheduled Visit
CTA[1]	X	X	X	X	X	X	X

1. Alternative diagnostic imaging to replace CTA scans could include fluoroscopic angiography, magnetic resonance angiography (MRA), ultrasound, and X-ray.

Parameter	Preferred	Alternate
Slice Spacing and Slice Thickness	0.625 to 2mm (Thinner slices preferred)	3mm or less* *5mm slice thickness may be utilized if ***absolutely necessary*** on Pre-Procedure Imaging Only – Visit 1)
Superior Extent	Include carotid bifurcation and cervical portion of the internal carotid artery and vertebral arteries	
Inferior Extent	Lesser trochanter of femur	
Other Instruction	Patient to hold breath per institutional standards. If full extent of scan cannot be completed on a single scan acquisition, at least a 2-3cm overlap exists on multiple scan ranges.	
Contrast and Phases[2]	A Three-Phase CT is requested that includes Non-Contrast, Arterial Phase, and Delayed/Venous Phase. Standard non-ionic per intuitional standards	
Contrast Volume and Rate	Per institutional standards to ensure adequate opacification of requested range of aorta and aortic branch vessel origins	
Scan Delay	Threshold detect per institutional standards.	

Other Imaging Modalities for Follow-up

- Other imaging such as Ultrasound, XRAY, MRI and Angiography may compliment/replace CTA in some instances
- Please refer to Core Lab Site Manual for guidelines on other modalities



Unscheduled Time Points

- If a patient has medical imaging performed at an unscheduled visit, please submit to the Core Lab in the following circumstances:
  - There is no CTA scan for that visit window
  - If the imaging was performed due to an **AE**, preceded an **additional aortic procedure**, or due to a **potential device deficiency**
  - For all other reasons, please ask your Artivion PM prior to uploading

EDC

ARTIVION™ | **Arcevo™ LSA**
Hybrid Stent Graft System

Expectations for Data Entry

The ‘ABCs’ for EDC, eCRFs, and Data Expectations

- Overview of iMedNet EDC system
  - Access and password instructions
- How to register a new patient
- Layout and Schedule Visit grid
  - Record Status icons
- Overview of ARTIZEN eCRFs
- Entering eCRF data
  - Visit Information and Visit Continuation forms
  - Embedded tables (example): Procedure form Arcevo LSA
  - Subject log forms: AEs, PDs, Concom Meds, Additional Post-Op Proc
  - Site log forms: Pre-Screening Failure Log, Site PD Log
  - Uploading SAE source doc files
- Query management
- PI signatures
- Study Exit
- EDC Resources

iMedNet Review

About the Electronic Data Capture (EDC) system

- **WHO:** All research site personnel who are assisting with EDC data entry and/or approval, as documented on the delegation of authority log (DOA)
- **WHAT:** The **iMedNet** EDC system uses electronic case report forms (eCRFs) to capture study and specific subject data
- **WHERE:** https://www.imednet.com/
- **WHEN:** EDC access will be granted by an Artivion team member *after the site is activated.* Study access to ARTIZEN is granted after completion of role-based training within the EDC system (video).
- **WHY:**
  - **Site Coordinators** to complete data entry into eCRFs, respond to queries, update and correct eCRFs
  - **Principal Investigator** to review and approve eCRFs
- **HOW:** See the next slides on how to access and enter data into the EDC system

Access Instructions

iMedNet – Initial user access

- EDC user access will be granted by an Artivion team member ***after*** **the site is activated**
- Once the user account is set up in EDC, the system will send out an automated email message to the user requesting password creation (see screenshot)

- This iMednet user email is sent from noreply@imednet.com

  → Check junk/spam/trash folders if the automated message is not found in the main email Inbox
- After changing the password, iMedNet can be accessed via the following link: https://www.imednet.com/
- Site users will be guided through a mandatory **system training video** within the EDC platform itself before gaining access to study data
  - No separate training is required prior to access being granted
- User accounts can only access the ARTIZEN study in EDC once the in-system training is completed

iMedNet – Create or change password

When creating or changing a password, the password must meet the following criteria:

- Must contain 10 - 50 characters
- Must include at least 3 of the following four-character types:
  - At least one uppercase letter (A–Z)
  - At least one lowercase letter (a–z)
  - At least one number (0–9)
  - At least one special character (Examples: " # & ' ( ) *)
- Must **not** contain the user's email address
- Must **not** include >2 identical characters in a row (eg, "aaa", "111")
- Must **not** be used as the previous 2 passwords

Please note:

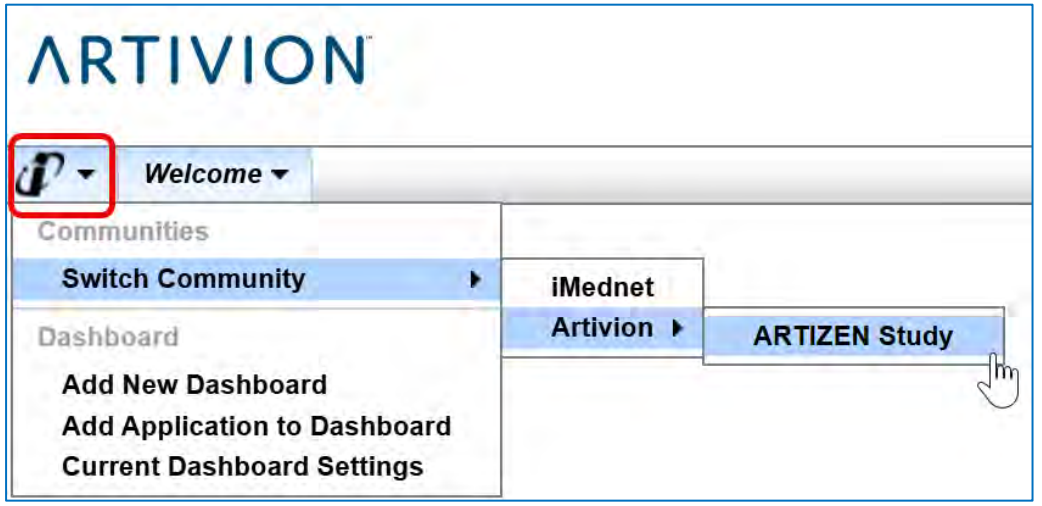
- In the event you do not remember your password, select the **Forgot Password** button (as shown in the image on the right)
- A user account is locked after 3 incorrect password attempts
- After the 3rd failed attempt, you will receive an email to reset the password.
- If you are locked out and need your password reset, you will have to contact **iMedNet** (support@imednet.com), as Artivion cannot reset EDC system passwords.

→ If you are unsure of your password, use the **Forgot Password** button so that you do not get locked out of your account

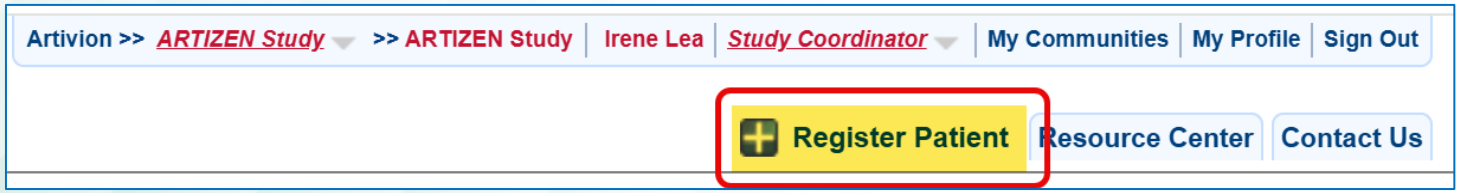
eCRFs

Registering a new ARTIZEN patient

- Log into iMednet via the following link: https://www.imednet.com/
- To access the ARTIZEN study under the **“i”** menu, select:
  Switch Community > Artivion > ARTIZEN Study

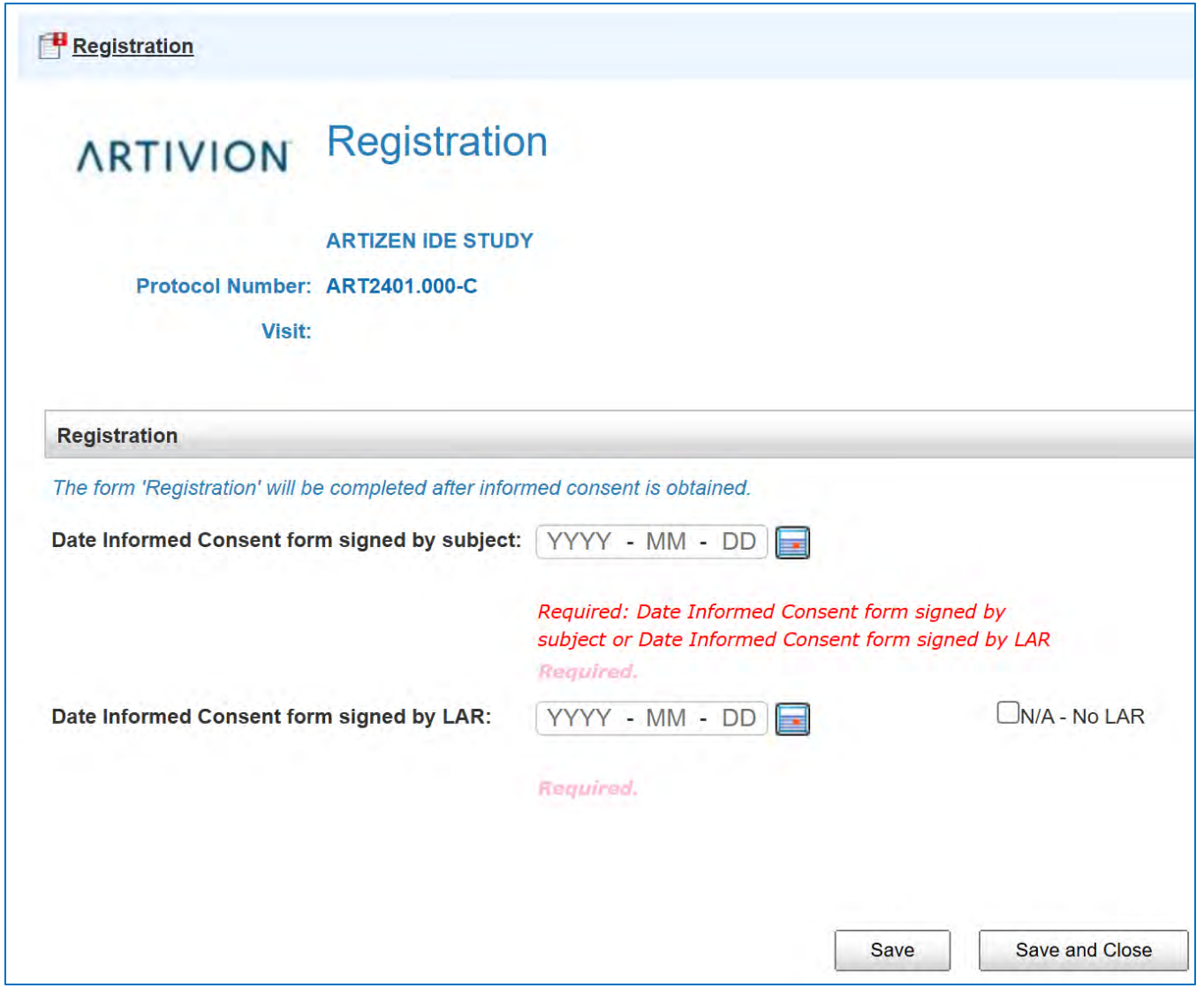


- To add a new patient to the study, click on the **+ Register Patient** button in the top right corner (below your username)



Registering a new patient (*continued*)

- Complete the information for the new patient on the **Registration** form
- In the bottom right corner, click the **Save** or **Save and Close** button
- Once closed, you will be at the patient's Record Page

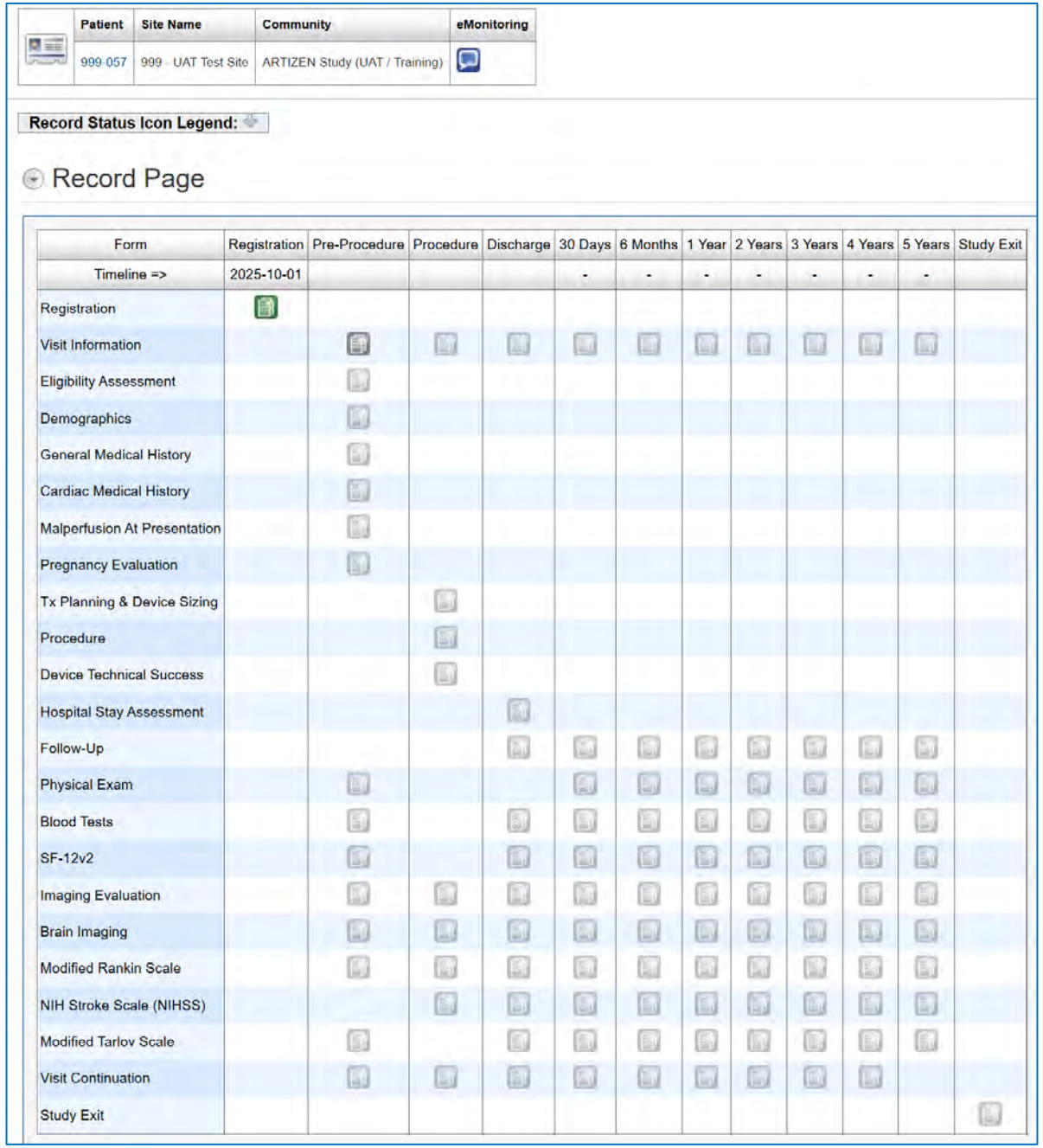


Visit schedule grid

The patient's **Record Page** shows all possible visits and the status of the forms

Note that the following patient log forms are *not* part of this visit schedule grid:

- o Concomitant Medications
- o Adverse Event
- o Protocol Deviation
- o Additional Post-Op Procedure



Patient	Site Name	Community	eMonitoring
999-057	999 - UAT Test Site	ARTIZEN Study (UAT / Training)	

Record Status Icon Legend:

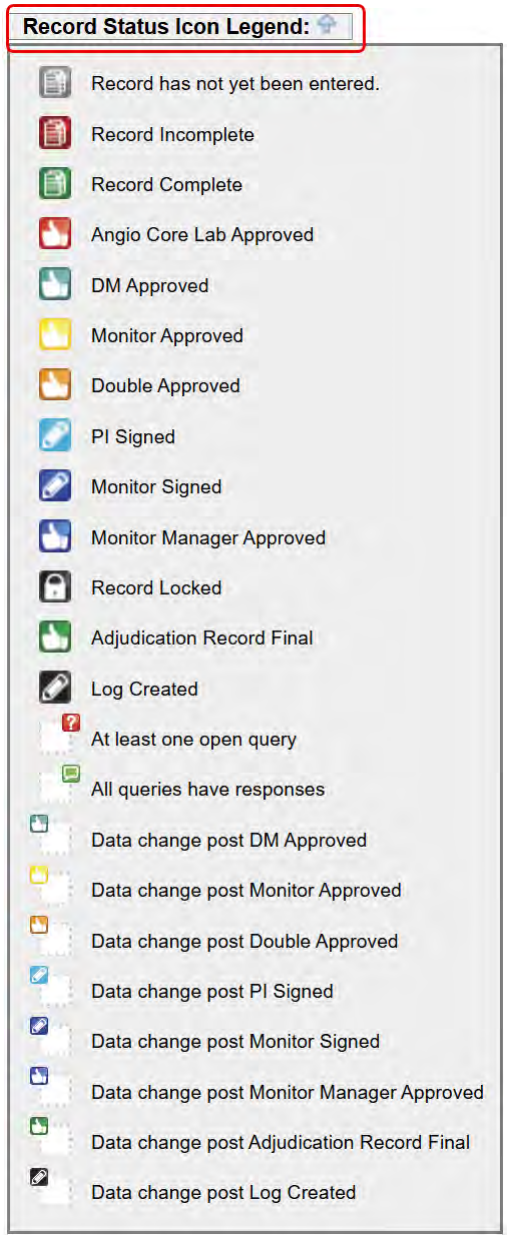
Record Page

Form	Registration	Pre-Procedure	Procedure	Discharge	30 Days	6 Months	1 Year	2 Years	3 Years	4 Years	5 Years	Study Exit
Timeline =>	2025-10-01				-	-	-	-	-	-	-	
Registration												
Visit Information												
Eligibility Assessment												
Demographics												
General Medical History												
Cardiac Medical History												
Malperfusion At Presentation												
Pregnancy Evaluation												
Tx Planning & Device Sizing												
Procedure												
Device Technical Success												
Hospital Stay Assessment												
Follow-Up												
Physical Exam												
Blood Tests												
SF-12v2												
Imaging Evaluation												
Brain Imaging												
Modified Rankin Scale												
NIH Stroke Scale (NIHSS)												
Modified Tarlov Scale												
Visit Continuation												
Study Exit												

Record Status Icon Legend

- The top of each **Patient Record Page** identifies the **Patient** and **Site Name**

- There is also a **Record Status Icon Legend** that can be expanded by clicking the down arrow to display all of the symbols used in this study grid. The complete listing is shown on the right. Note that the symbols may be different based on your EDC role.



Overview of ARTIZEN eCRFs

- In total, there are 29 unique eCRFs which may require site data entry (see list below)
- Some eCRFs are associated with a visit and appear under the appropriate visit, and some eCRFs are only completed as applicable and are unplanned

Forms associated with a visit

- Registration
- Study Eligibility
- Demographics
- General Medical History
- Cardiac Medical History
- Malperfusion At Presentation (acute dissection only)
- Pregnancy Evaluation (female only)
- Concomitant Medications (log form)
- Physical Exam
- Blood Tests
- SF-12v2
- Imaging Evaluation
- Brain Imaging
- Modified Rankin Scale
- Modified Tarlov Scale
- NIHSS
- Tx Planning & Device Sizing
- Procedure
- Device Technical Success
- Hospital Stay Assessment
- Visit Information
- Visit Continuation
- Follow-up
- Study Exit

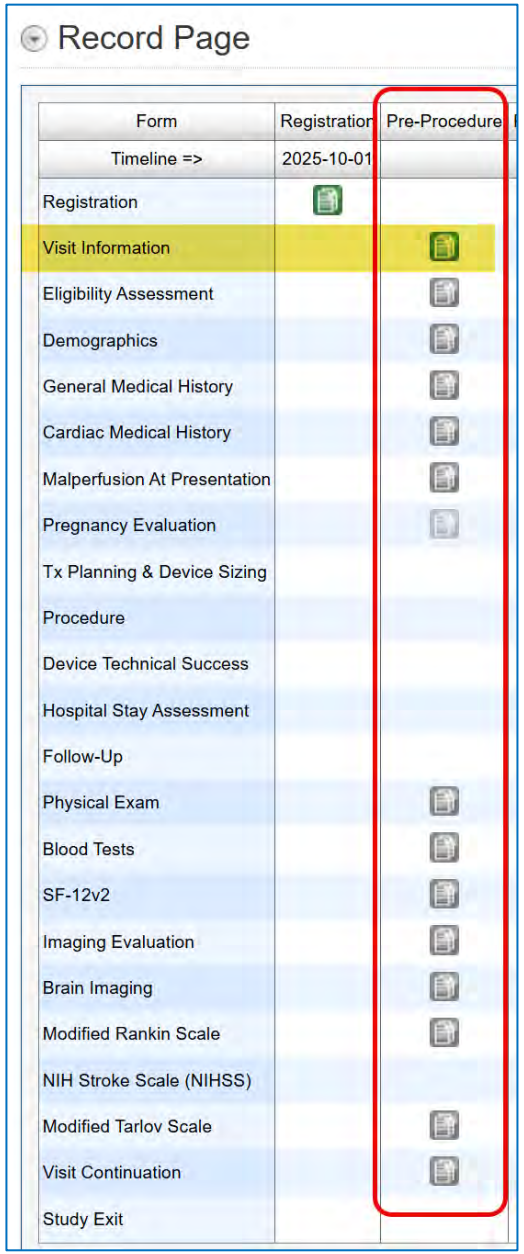
Forms completed ad hoc

- Pre-Screening Failure Log
- Additional Post-Op Procedures
- Adverse Events
- Protocol Deviations
- Site PD Log

NOTE: Core Lab forms are read-only for sites

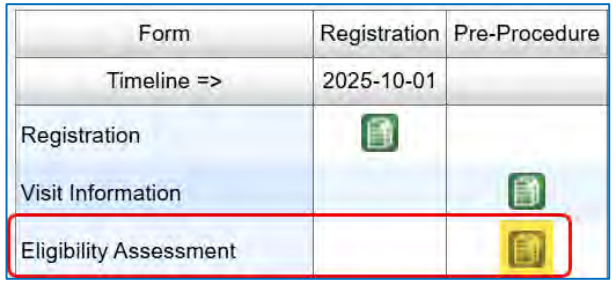
Visit Information and Visit Continuation forms

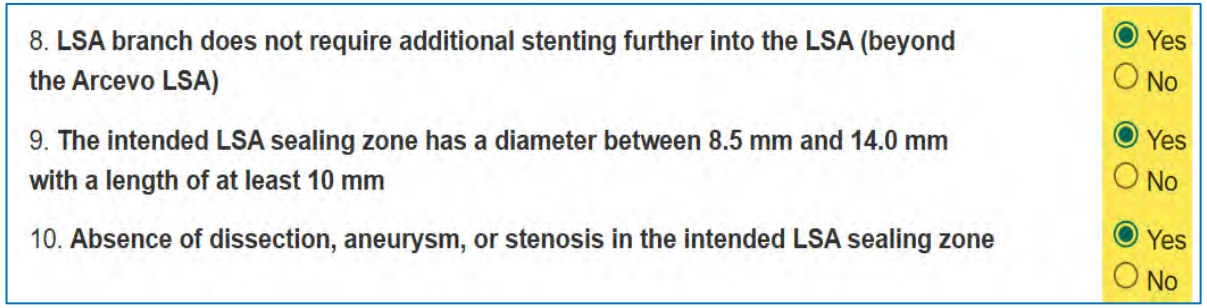
- Complete the **Visit Information** form **FIRST**
  - The first question of 'Was the visit performed?' must be YES in order to activate the *rest of the forms for that visit* in EDC
  - The screen shot on the right has the **Pre-Procedure** visit as an example with the following:
    - Completed **Visit Information** form (green Record Complete status icon)
    - The remainder of the visit forms (incl. **Eligibility Assessment**, **Demographics**, medical history forms, **Malperfusion at Presentation**, and other assessment forms) are new forms that can now be entered
    - **Pregnancy Evaluation** is grayed out as it will only appear after **Demographics** form is completed for female patient
- Complete the **Visit Continuation** form last
  - The first question of 'Is the subject expected to continue participation in the study?' must be YES in order to activate the *next visit* in EDC
  - Note that certain visits (eg, Procedure and Discharge) have *additional* conditions/requirements for triggering the next visit in EDC

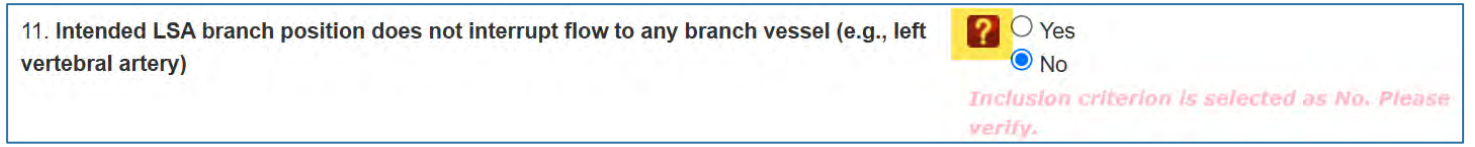


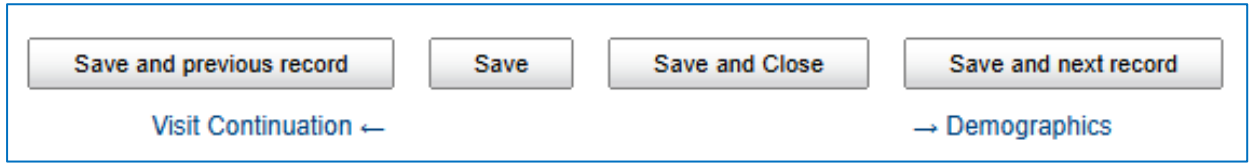
Entering eCRF data

- From the **Record Page** (visit schedule grid), select the Record (clipboard) icon of the form you want to enter data in
- Enter data into EDC by answering each question/completing each field
  - Blue call-out bubbles show your EDC data entry selection for radio buttons
  - To de-select a radio button, hold down the **<Shift>** key while clicking the selection)
- Any question with an unanswered query appears with a red **?** and *red query text*
- At the end of the form, choose one of the **Save** button options at the bottom of the form



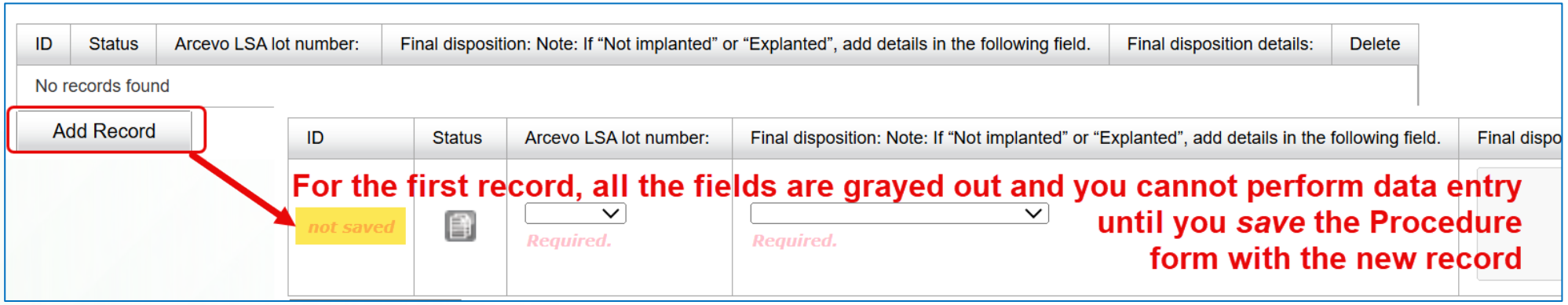






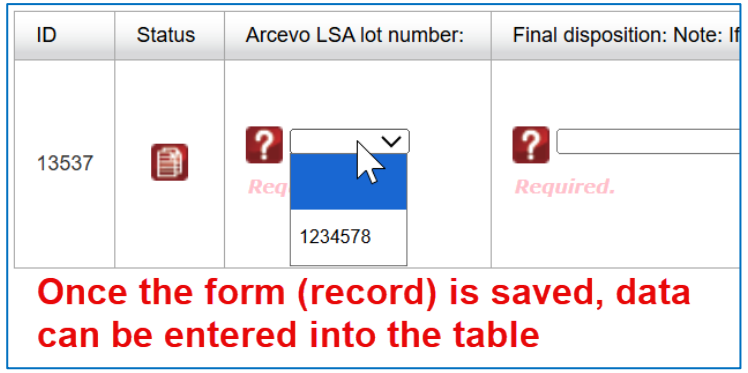
Embedded table: Procedure form Arcevo LSA table

An **embedded table** contains an additional sub-form and data fields. The **Procedure** form below shows the embedded table for the **Arcevo LSA.**



To add the **first** row into an embedded table:

1) Click the **Add Record** button to add the new row.
2) You must ***save*** the eCRF for the first row.
3) Once the row is added to the table, you can enter data.
4) For the ‘Arcevo LSA lot number’ drop-down list, if there are no available devices listed, ensure that your site has acknowledged receipt of a shipment in the **Inventory** module: iMenu > Inventory > Arcevo LSA Inventory Catalog > Shipments

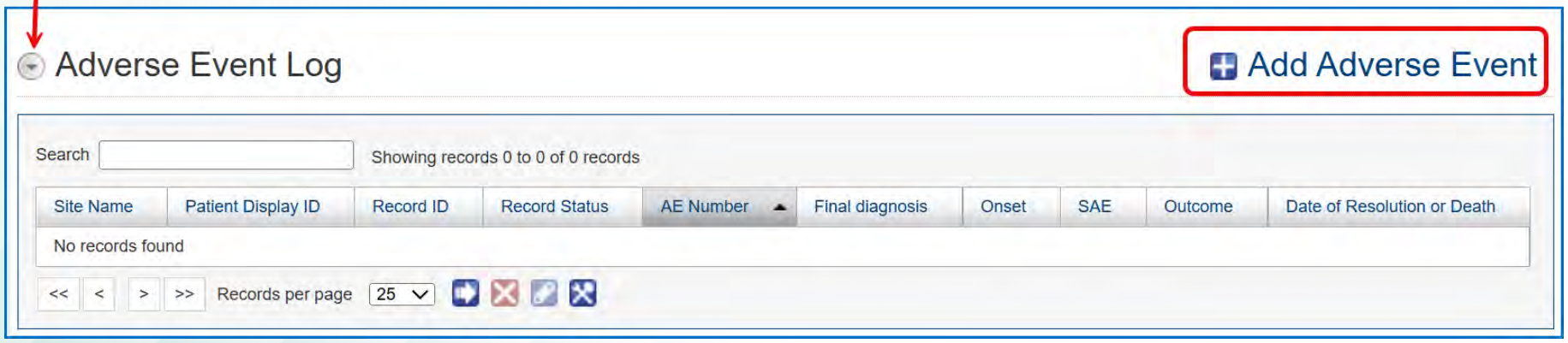


ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Patient Log forms:
Concomitant Meds, Additional Post-Op Procedure, AEs, PDs

- Patient log forms are in a separate table (**Patient Record Reports**) located **below** both the main visit schedule grid and the Core Lab forms.
- Select the form you want (e.g., **Adverse Event Log**) and the corresponding log appears.

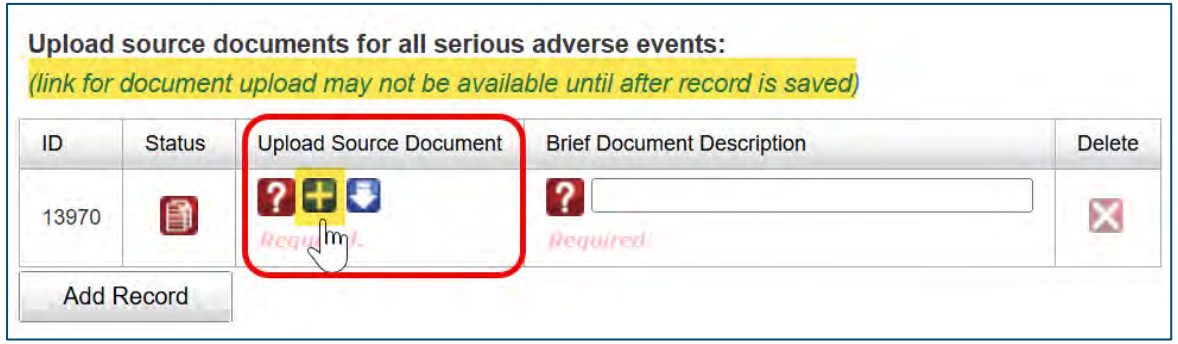
- To add a new AE form, click on the **+Add Adverse Event** button on the far right of the log table
  - If you cannot see the +Add button, scroll all the way to the right of your screen (esp. for the **Concomitant Medications** log)
- A new **Adverse Event** form will then open for data entry

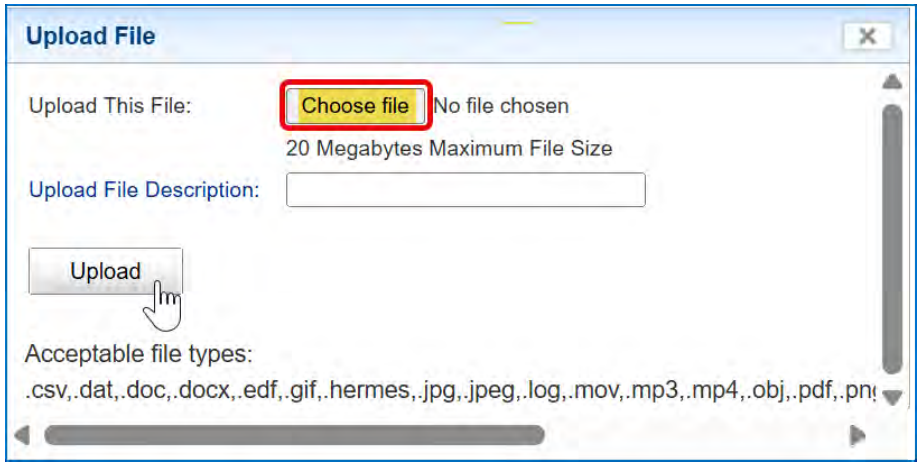


ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Uploading SAE source docs (another embedded table)

- Upload source documents for all SAEs (not for every AE). Ensure all uploaded documents are ***de-identified.***
- To upload the **first** file into the **Source Documents** table:
  1) Click the **Add Record** button to add the new row.
  2) You must ***save*** the **Adverse Event** eCRF.
  3) Once the row is added to the table, you can upload documents by clicking the **+** button
  4) Complete the **Upload File** dialog box fields:
     a) For 'Choose file' selection:
        - Maximum file size: 20MG
        - Acceptable file types: .csv, .dat, .doc, .docx, .edf, .gif, .hermes, .jpg, .jpeg, .log, .mov, .mp3, .mp4, .obj, .pdf, .png, .ram, .tif, .txt, .wav, .xls, .xlsm, .xlsx, .xml, .xm_, .zip
     b) Enter text for 'Upload File Description'
     c) Click the **Upload** button

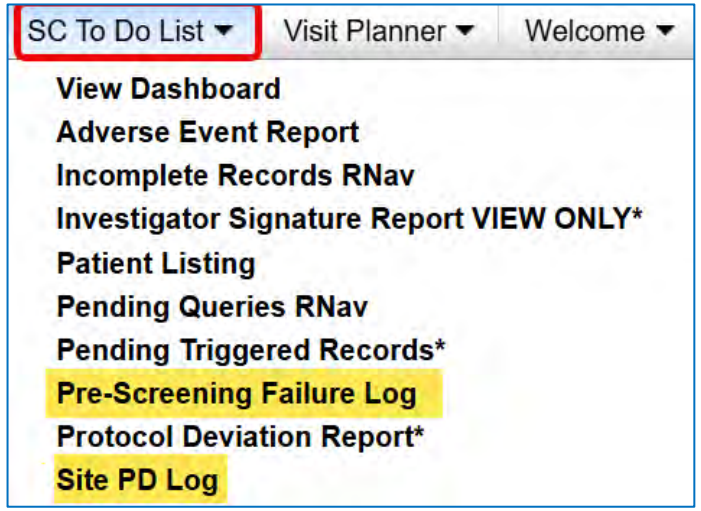


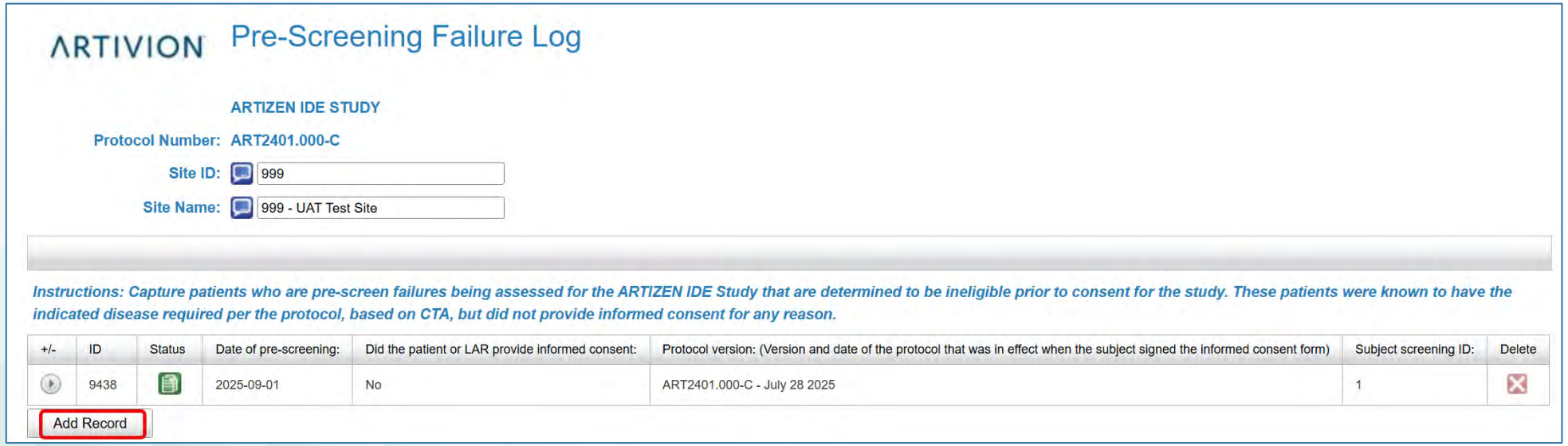


Site-entered Log forms:
Pre-Screening Failure Log and Site PD Log

There are 2 site-entered log forms accessed from the role-specific **To Do List** tab at the top of the page

- The screen shot on the right shows the **SC To Do List** for the Study Coordinator (SC) role
- Add new rows to the **Pre-Screening Failure Log** form by clicking the **Add Record** button

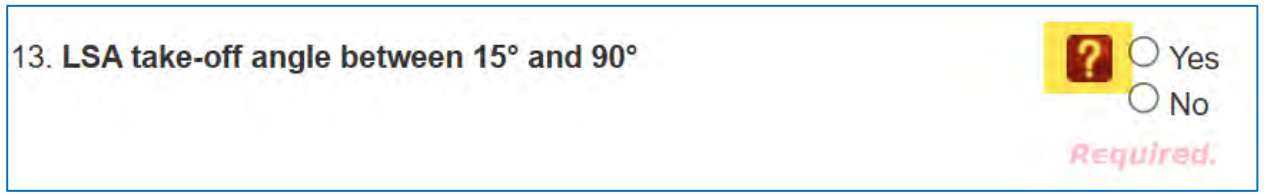




ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Query management

- Open queries are identified by a question mark **?** icon next to the field



- The type of query will be indicated by a different color for the **?** icon:
  - Red system auto query
  - Orange Monitor query
  - Yellow DM query
- There are two steps to resolving an open query:
  1) Responding to the query
  2) Updating the data value in EDC (as applicable)

- **Note:** Auto queries with a red ? will normally close automatically once the data is updated. However, if an auto query still remains open (i.e., data is correct as entered/updated), then a query response is still needed as shown on the next page.

Query management (*continued*)

Step 1: Responding to the open query

a) Next to the field, click on the open orange Monitor query icon

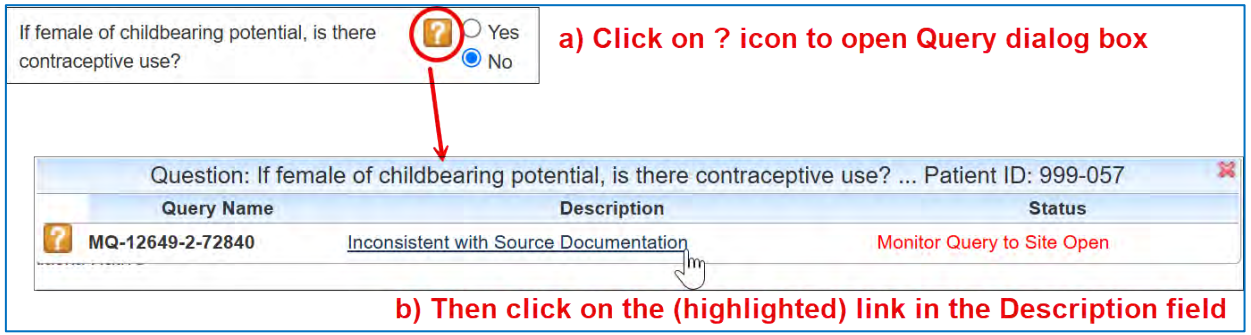
b) This will open the larger query dialog box; click on the link in the 'Description' field

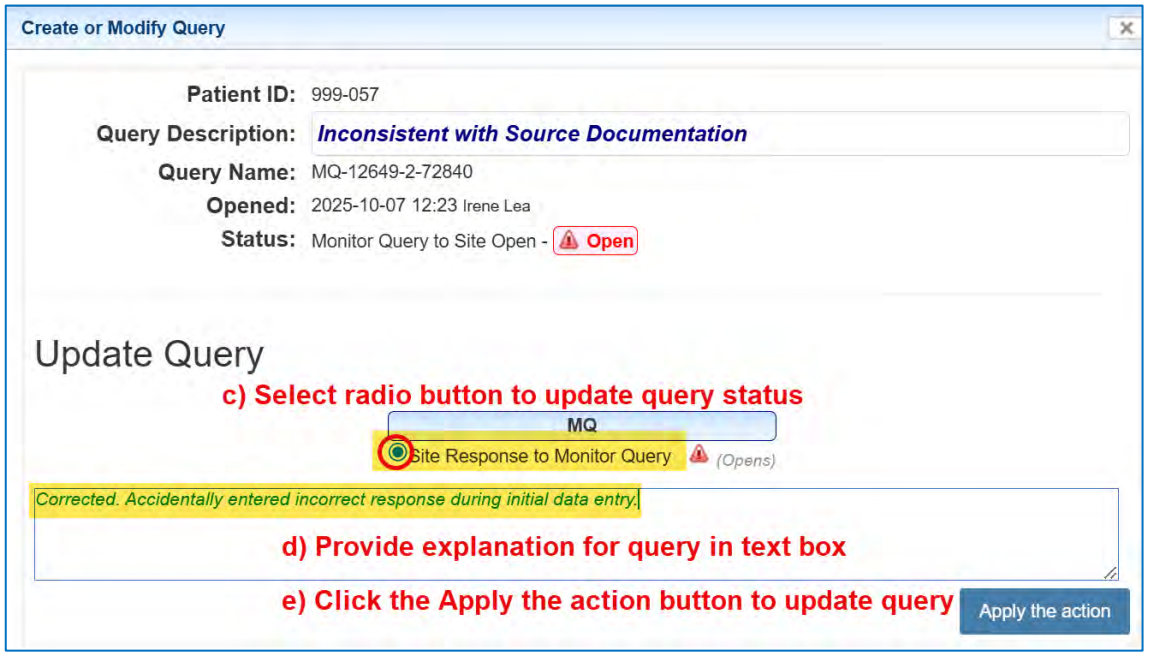
c) Update the query status

d) Also provide a brief explanation for the query response/updates

e) Click the **Apply the action** button

f) The query icon updates to reflect the updated status





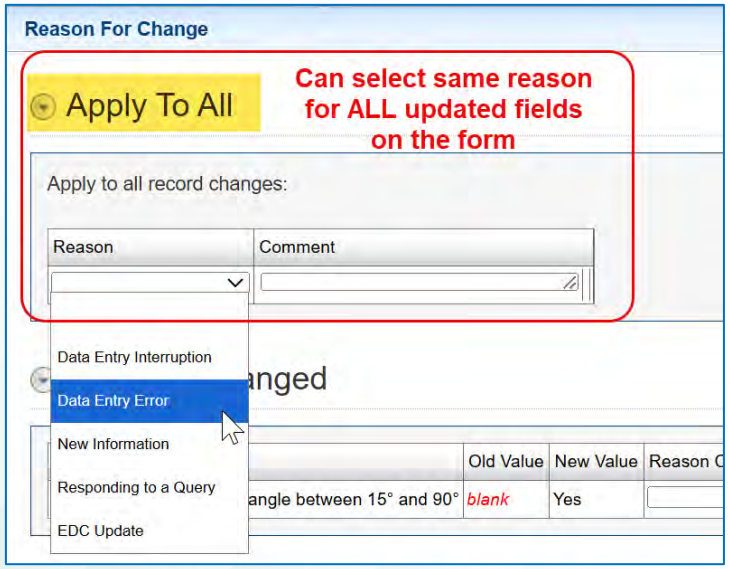
Query management (*continued*)

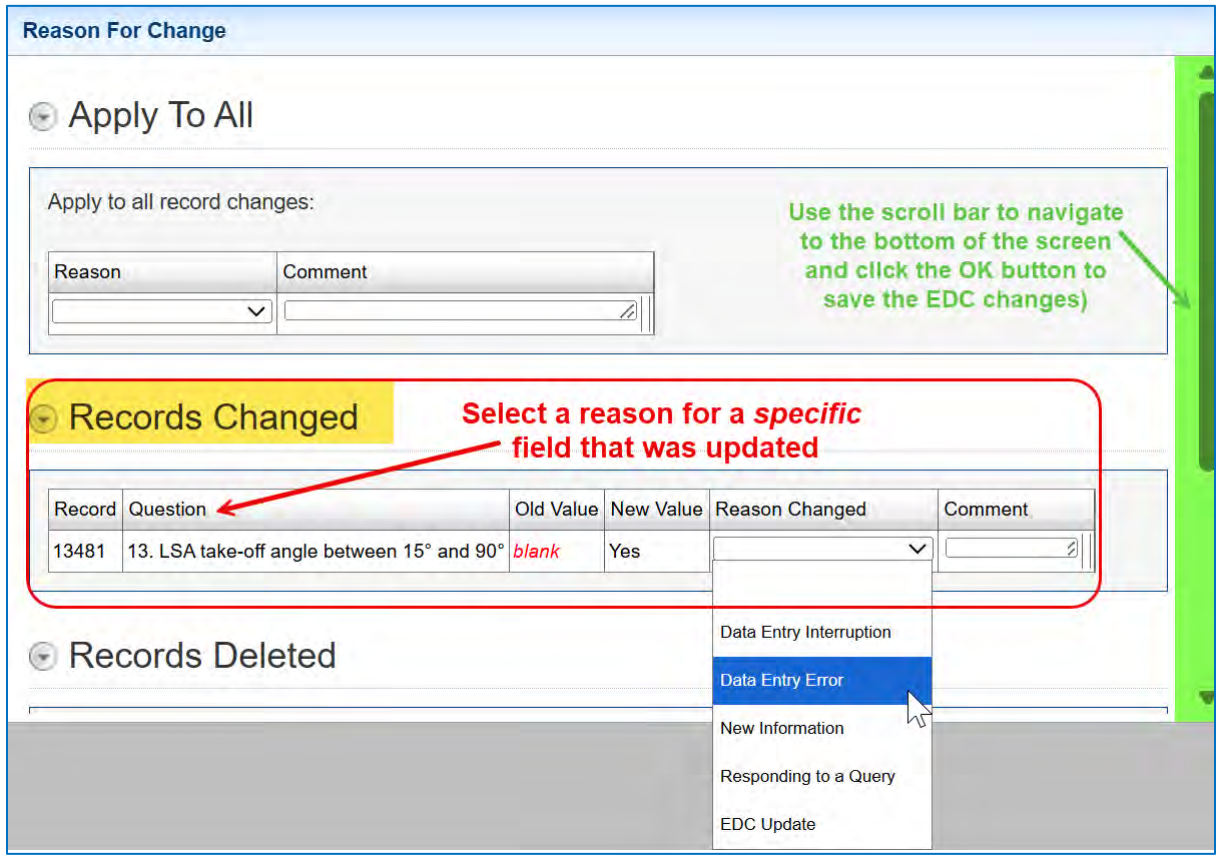
Step 2: Updating the data value in EDC

a) After updating a field in EDC, the **Reason for Change** dialog box appears when saving

b) Updating the action taken to address this query by completing 'Reason for Change'

c) Add a reason from the drop-down menu and provide a comment, if applicable

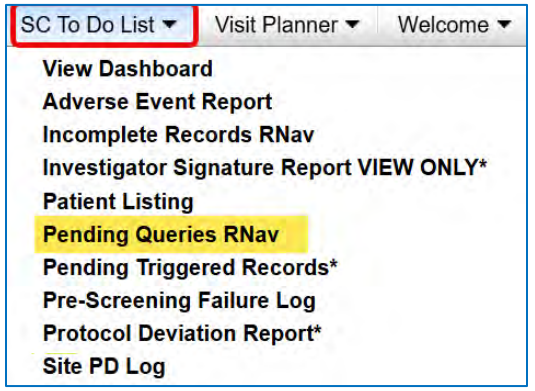


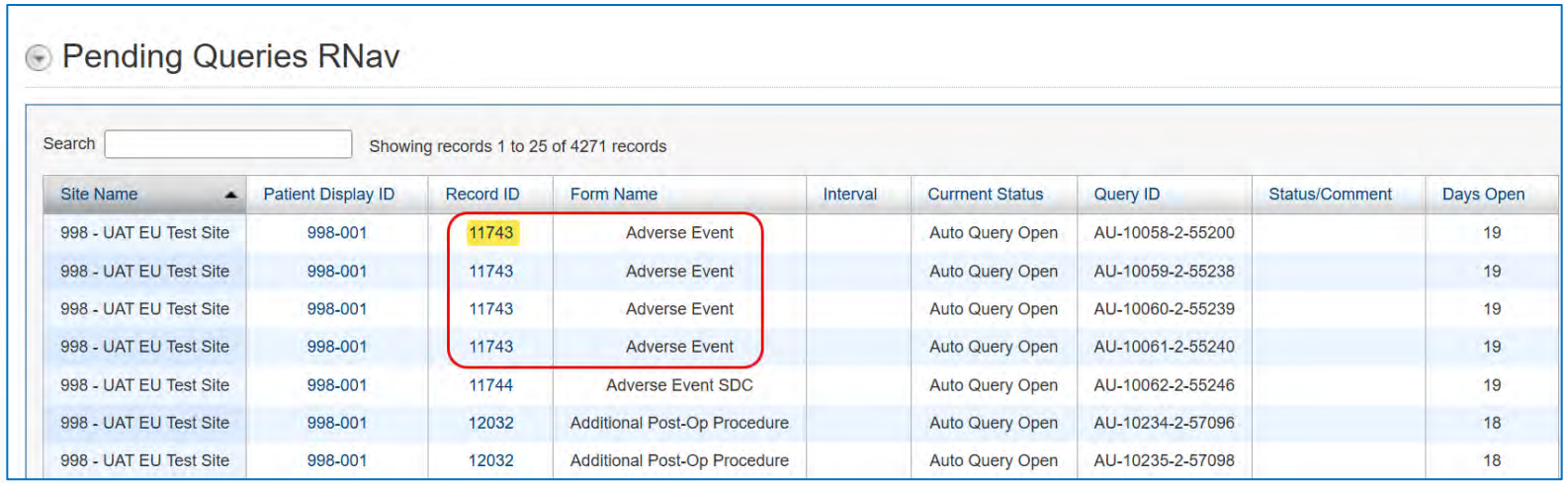


d) Use the scroll bar on the right to scroll to the bottom of the window and click the **OK** button to save

Query management (*continued*)

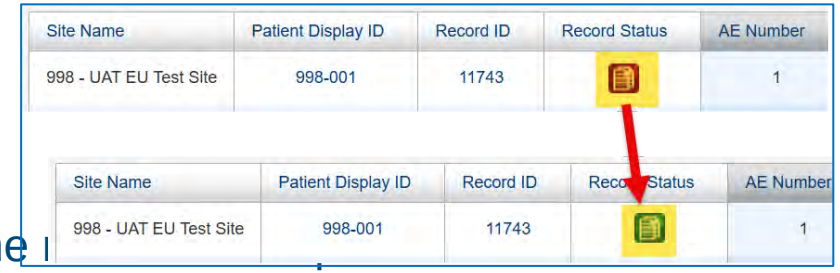
- From the **SC To Do List** tab in the top left, select **Pending Queries RNav** from the drop-down menu
- This will show all open queries with associated information





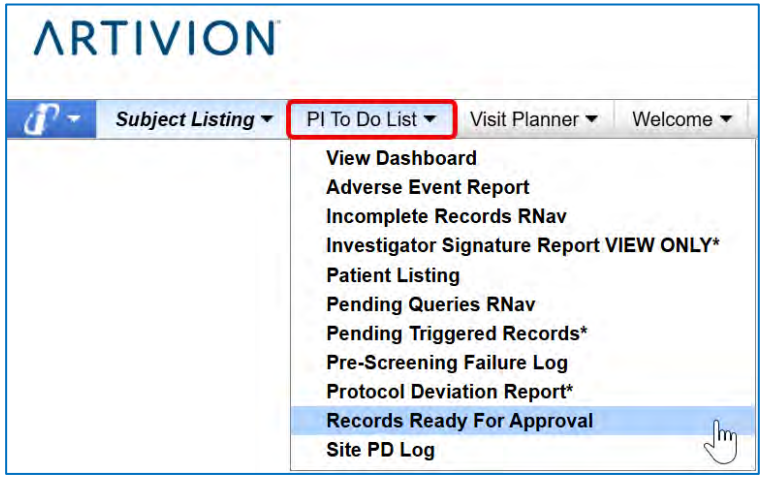
Site Name	Patient Display ID	Record ID	Form Name	Interval	Currnent Status	Query ID	Status/Comment	Days Open
998 - UAT EU Test Site	998-001	11743	Adverse Event		Auto Query Open	AU-10058-2-55200		19
998 - UAT EU Test Site	998-001	11743	Adverse Event		Auto Query Open	AU-10059-2-55238		19
998 - UAT EU Test Site	998-001	11743	Adverse Event		Auto Query Open	AU-10060-2-55239		19
998 - UAT EU Test Site	998-001	11743	Adverse Event		Auto Query Open	AU-10061-2-55240		19
998 - UAT EU Test Site	998-001	11744	Adverse Event SDC		Auto Query Open	AU-10062-2-55246		19
998 - UAT EU Test Site	998-001	12032	Additional Post-Op Procedure		Auto Query Open	AU-10234-2-57096		18
998 - UAT EU Test Site	998-001	12032	Additional Post-Op Procedure		Auto Query Open	AU-10235-2-57098		18

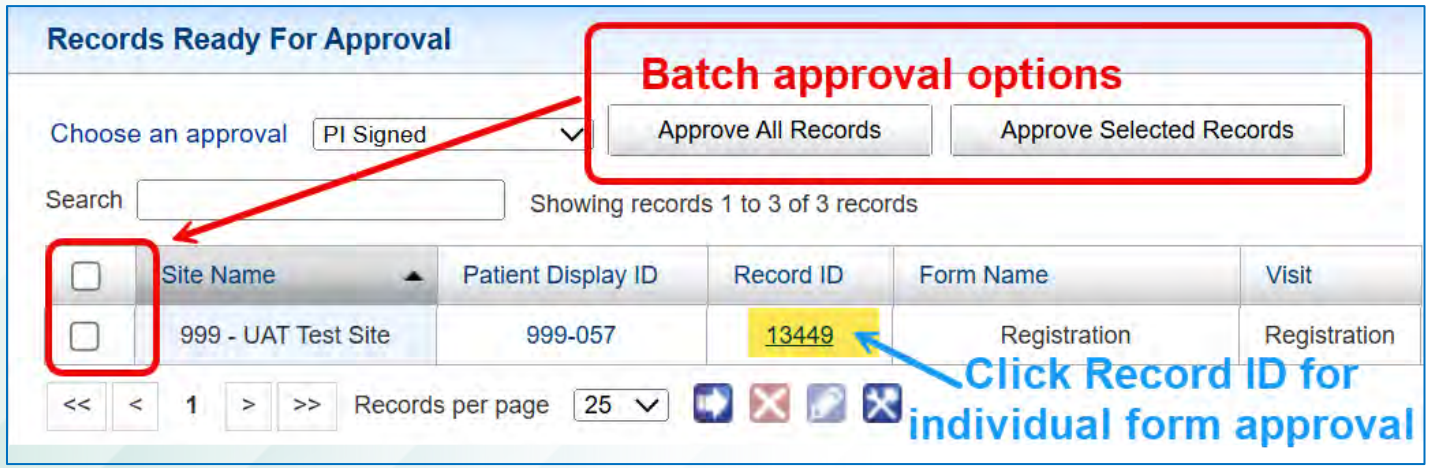
- Clicking on the Record ID (11743) will take you to the specific form (record) with the open query. In the example above, this AE form has 4 open auto queries and each query is listed separately.
- Scroll through the entire AE form to address all open queries
  - Respond to each query, update query status, provide explanation
  - If data is updated, provide Reason for Change
- Once all queries are addressed and saved, then back on the subject's Record Page - the record status (clipboard) icon for that form has changed from red (incomplete) to is green meaning that the f



PI signatures

- PI signatures will be required prior to planned database locks
- From the '**PI To Do List**' tab, select **Records Ready for Approval** from the drop-down menu
- Select forms (records) to be signed
  - o Batch approval options (for all or selected)
  - o Individual form approval
- Use iMednet password for PI signature approval
- PIs will receive instruction at the time of the request

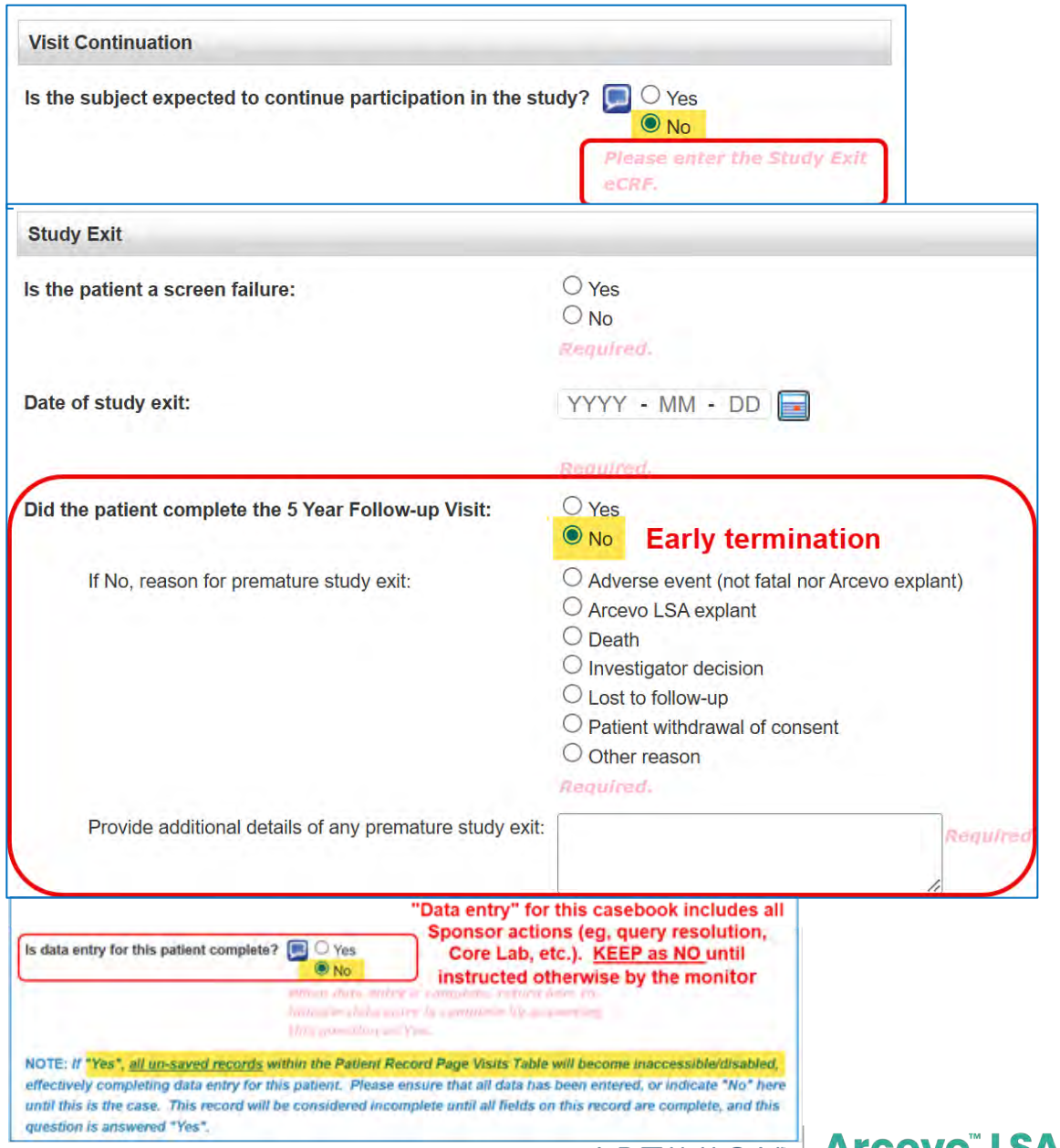




ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Study Exit form

- The **Study Exit** form is activated from the **Visit Continuation** form when 'Is the subject expected to continue participation in the study?' is answered with 'No'
  - If a patient early exits the study due to an AE, go to the next expected visit for the subject to update the **Visit Continuation** form
- For early terminations on the **Study Exit** form, enter 'Did the patient complete the 5 Year Follow-up Visit' as 'No'
- The last question on the **Study Exit** form 'Is data entry for this patient complete' should **remain 'NO'** until ALL data entry, monitoring, queries, and review have been completed
  - Once this last field is answered as 'Yes' → **NO MORE CHANGES can be made in EDC** for this patient (including for Core Lab, CEC, etc.)
- The Artivion monitor will provide guidance as to when this last field should be changed to 'Yes'



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Resources

EDC Resources

- This IM presentation provides an overview for EDC and study-specific details for intended data collection
- The iMedNet training video is meant to provide role-specific functionality in EDC
- ***eCRF Completion Guidelines*** will be provided to all sites and will serve as the most detailed resource for questions about the eCRFs and basic EDC functionality
- For any technical issues with iMednet access (including password resets), contact:
  - **iMednet Customer Support**
  - **E-mail:** support@imednet.com
  - **Phone Number:** (866) 258-2735
  - **iMednet's Support Hours:** Monday-Friday, 7:00 am to 5:30 pm US Central Time
- If you have any study-specific questions related to the EDC, please contact your Artivion monitor

19. What should you do if you can't remember your iMednet password?

20. What do you do if you cannot enter data in the first form (row) of a log table?

21. What do you do if you cannot enter data in the first form (row) of a log table?

Safety Processes

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

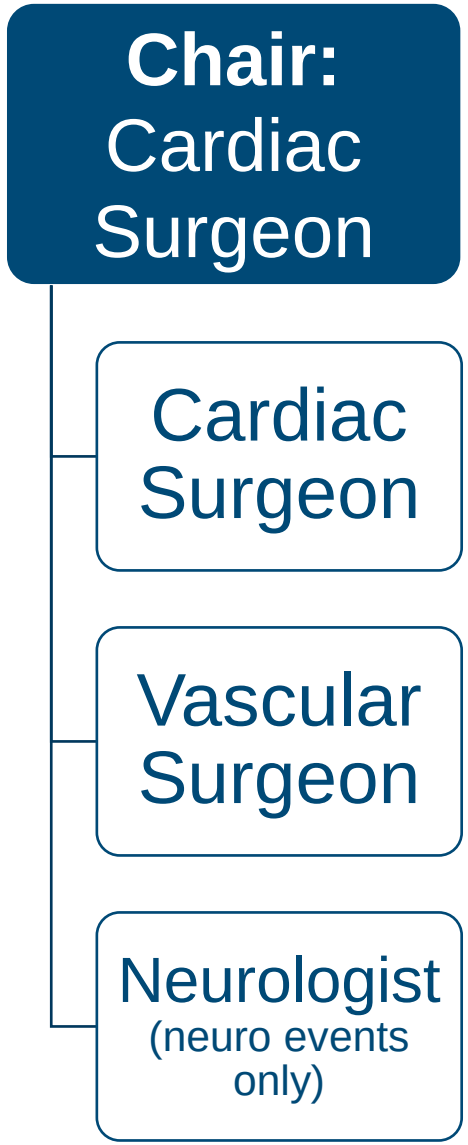
Roles and Responsibilities

Roles and Responsibilities

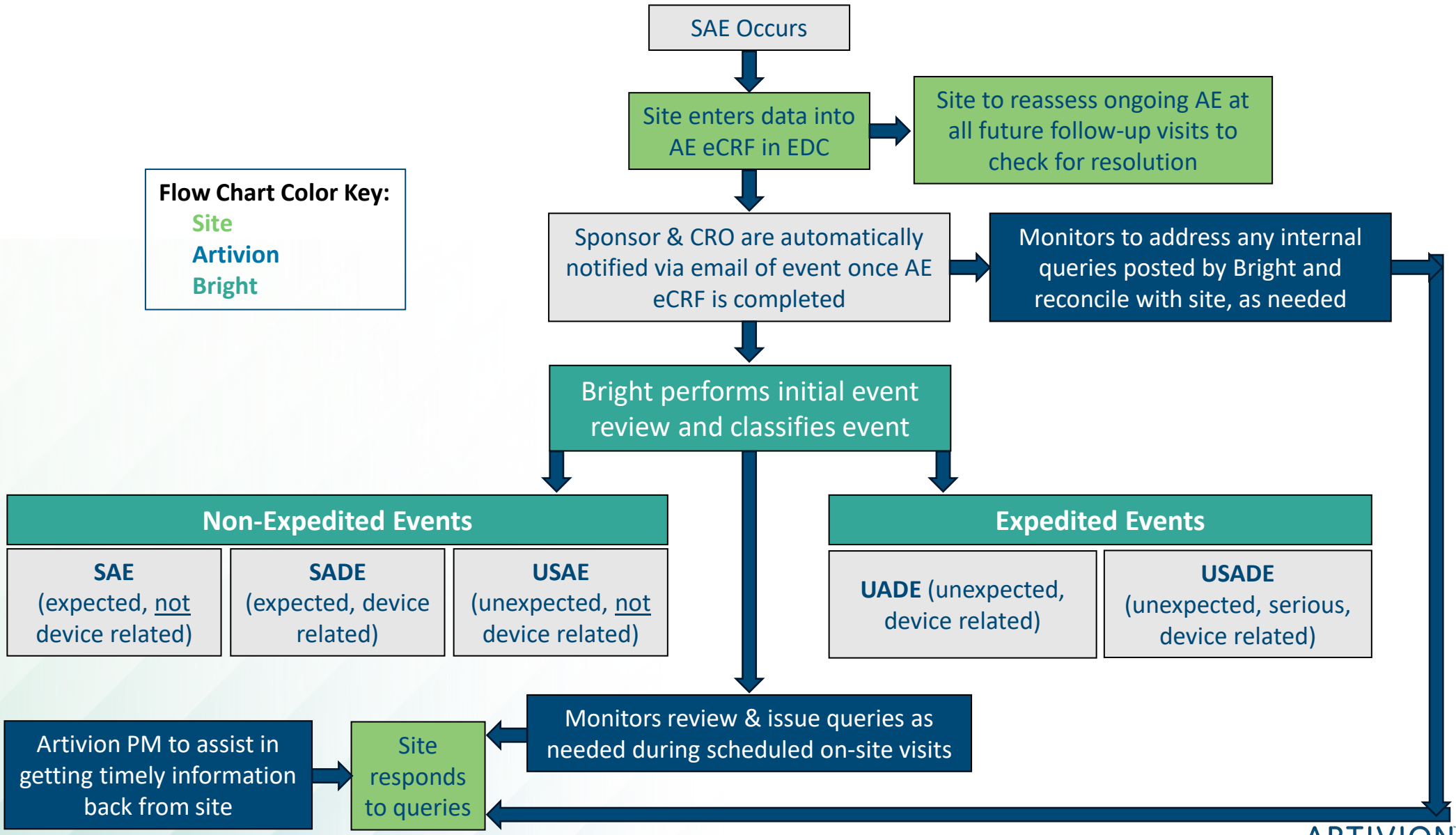
Sponsor	
Artivion PM	• Manage safety review and reporting process • Review safety event narratives
Artivion Monitor	• AE review and query management with the sites • Collect redacted source documents, as needed
CRO	
Bright Research	• Perform data review on all safety events reported by sites • Initial review for safety event designation • Compile information for the Safety Event Narrative • Review and facilitate AE adjudication, as needed • Review reported adverse events (AEs) and code all events using MedDRA coding module

Clinical Events Committee (CEC)

- CEC is an independent group of experts that provides an objective assessment of clinical trial endpoints or events and helps to ensure the credibility and reliability of trial results
- The ARTIZEN CEC will independently review and determine whether specific events or endpoints have occurred during the clinical trial, based on predefined criteria in the protocol, the CEC charter, and the Statistical Analysis Plan (SAP)
- 4-person committee (see membership on the right)
- Members are selected from sites that are *not* participating in ARTIZEN and based on member experience



Safety Event Processing Workflow



ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Definitions

Definitions

Adverse Event (AE)

- Any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device or Valiant Captivia.
- This definition includes events related to the procedures involved.
- For users or other persons, this definition is restricted to events related to the use of the investigational medical device.

Adverse Device Effect (ADE)

- An adverse effect related to the use of an investigational medical device.
- Includes AEs resulting from insufficient or inadequate IFU, deployment, implantation, installation, operation, or any malfunction of the investigational medical device.
- Includes any event resulting from use error or from intentional misuse of the investigational medical device.

Definitions (cont.)

Serious Adverse Event (SAE)

- Any adverse event that led to any of the following:
  - Death
  - Serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
    - A life-threatening illness or injury, or
    - A permanent impairment of a body structure or a body function including chronic diseases, or
    - In-patient or prolonged hospitalization, or
    - Medical or surgical intervention to prevent life-threating illness or injury, or permanent impairment of a body structure or body function
  - Fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment

Hospitalizations or medical / surgical intervention (known pre-procedure) for a pre-existing condition is not considered an SAE

Definitions (cont.)

Serious Adverse Device Effect (SADE) / Unanticipated Serious Adverse Device Effect (USADE)

- An SADE is an ADE that has resulted in any of the consequences characteristic of an SAE.
- Can be either anticipated or unanticipated.
- An anticipated SADE is an effect which by its nature, incidence, severity, or outcome has been identified in the current risk assessment, IFU, ICF, and study protocol.
- An unanticipated SADE (USADE) is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subject.

Definitions (cont.)

Device Deficiency (DD)

- An inadequacy of a medical device related to its identity, quality, durability, reliability, safety, or performance. Device deficiency includes malfunction, misuse or use errors, and inadequate labeling.

- **Device deficiencies *not related to an adverse event*** include issues with packaging, labeling, device, or usability and includes some of the following examples:
  - Defective delivery system or implant
  - Issue with removal of Arcevo LSA from packaging
  - Issue with implantation (i.e., insertion, deployment, withdrawal)
  - Missing item from box
  - Labeling or packing issue
    - Reporting is initiated by site data entry into the Procedure eCRF.
    - If a deficiency is identified after the procedure, please e-mail information to your Artivion PM

Reporting Requirements

Adverse Events Documentation

- Document in the Adverse Event eCRF (no paper form to email)
- Upload redacted source documents for all SAEs directly into the AE eCRF
- Reportable from time of index procedure to study exit
- Death is an outcome, please enter the cause of death as the AE in the AE eCRF
    - The only reason death should be entered as an AE is if there is no information available on cause of death
- If an AE led to an additional procedure, ensure that the procedure is completed on the Additional Post-Op Procedure eCRF

Adverse Events Documentation (cont.)

- **Relatedness:** Investigators determine relatedness to Arcevo LSA device, Arcevo procedure, and Valiant Captivia device (as applicable):
  - **Unrelated:** AE is due to the underlying disease state or is due to concomitant medications or therapy not related to the use of the device.
  - **Possibly:** AE has a reasonable temporal relationship to the use of the device, but alternative etiology is equally or more likely compared to the potential relationship to the use of the device.
  - **Probably:** AE has a strong temporal relationship to the use of the device and alternative etiology is less likely compared to the potential relationship to the use of the device.
  - **Definitely:** AE has a strong temporal relationship to the use of the device, follows a known response pattern and cannot reasonably be explained by known characteristics of the subject's clinical state or other therapies.

US Reporting Requirements

AE Type	Submitted To	Requirement
Serious Adverse Event (SAE)	Sponsor/CRO	**Subject Deaths:** Notification must be made within 3 working days after the site is made aware of the event. **Other SAEs:** Notification must be made within 5 working days after the site is made aware of the event.
	IRB	Per IRB reporting requirements.
Unanticipated Adverse Device Effects (UADE)	Sponsor/CRO & IRB	Notification as soon as possible, but no later than 10 working days after the investigator first learns of the effect.
Device Deficiency (DD) that might have led to an SAE if appropriate action had not been taken, intervention had not occurred, or circumstances had been less fortunate	Sponsor/CRO	Notification without unjustified delay after the investigator first learns of the device deficiency that might have led to an SAE.

22. Which of these events does not require adjudication by the CEC?

Events Requiring Adjudication

Events Requiring Adjudication

- Events of interest that support endpoints as defined in the protocol will be adjudicated by the Clinical Events Committee (CEC)
- Sites may need to provide source documents (SDs) to assist with adjudication
- Artivion or the CEC may determine that an event not initially intended for adjudication requires it

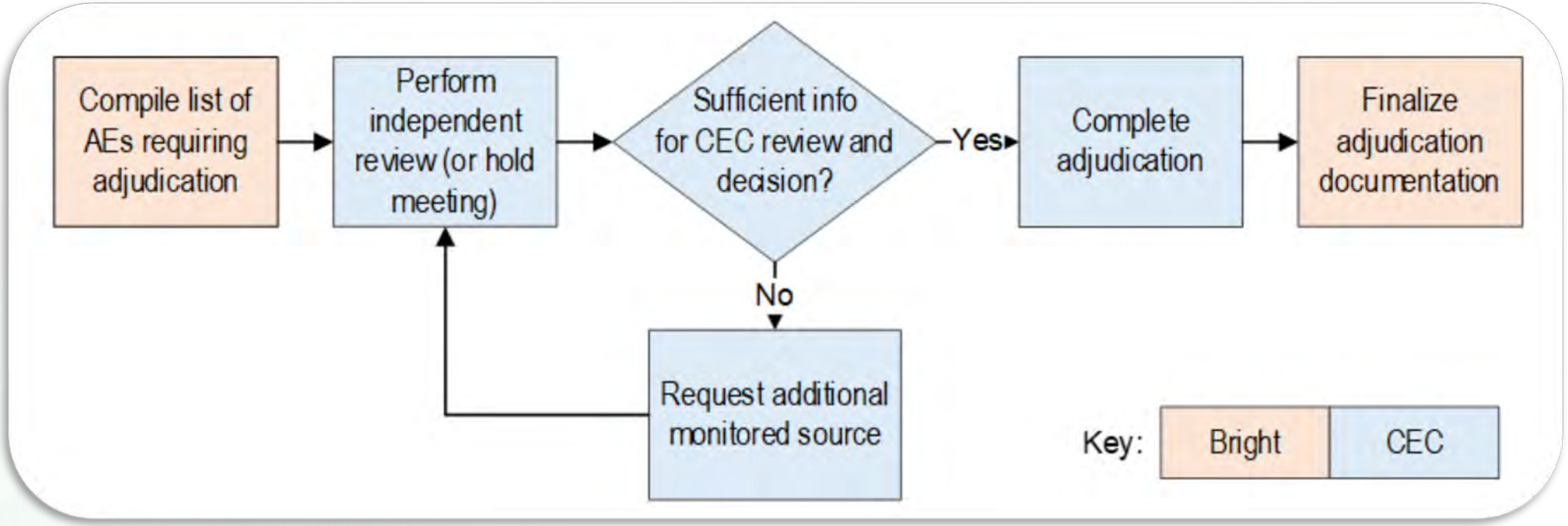
- Additional aortic procedure(s) (planned or unplanned, reoperation or not, in the treated segment or not)
- Any stroke (disabling or non-disabling)
- Aortic rupture
- Arcevo LSA explant
- Bowel ischemia
- Death (for any reason)
- Hypersensitivity
- LSA occlusion
- Myocardial infarction (MI)
- Paraplegia or paraparesis

- Pseudoaneurysm
- Recurrent laryngeal or phrenic nerve injury
- Renal failure requiring dialysis
- Respiratory failure
- Secondary procedures related to TEVAR extension
- Transient ischemic attack (TIA)
- All reported SAEs that are considered by the Investigator as at least possibly related to Arcevo LSA
- Any AE that may be associated with a DD

Reference Materials Needed from Sites

- Materials that will be available to CEC members for each AE requiring adjudication:
  - Subject summary:
    - Demographics, medical history, and procedure summary including treatment arm
    - Site-reported AE information including diagnosis, SAE determination, event description, onset date, outcome, relatedness determination, and action or intervention taken
  - Copy of AE CRF
  - Source documentation
  - Images submitted to the core lab, as needed

Adjudication Procedure



Sites will be responsible for:

- Ensuring sufficient AE data is entered into the EDC
- Upload additional de-identified source documentation, as needed
- Ensure imaging files are uploaded to AGMedNet
- Resolve/respond to queries in a timely manner

Data to be Adjudicated

CEC will adjudicate the following:

- **Final Diagnosis:** review and adjudicate the site's reported final diagnosis
- **Seriousness:** CEC will describe which criteria were met
- **Relatedness:** CEC will determine if an AE is related to the study device and/or procedure as defined by the protocol

CEC may decide that:

- An AE is not a reportable event,
- Two or more AEs should be merged into one event, or
- A single AE should be split into more than one event

CEC may decide to re-adjudicate an event if:

- There are changes or updates to AE diagnosis, relatedness, or seriousness
- There are changes to the subject's medical history that may affect causality of the reported AE
- Additional SD becomes available after the initial adjudication that may increase the severity of the event or indicate the AE is serious

Steps to Activation & Timeline Review

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Requirements to Activate

Site Activation

Sites will receive an activation letter when all the following are complete:

IRB Approval

- ❑ Receive Artivion approval of any ICF revisions
- ❑ Submit Artivion approved ICF to IRB
- ❑ Provide IRB approval documents
- ❑ If using local IRB – IRB roster

Required Study Documentation

- ❑ Submit completed W-9
- ❑ Submit Financial Disclosure for all Investigators
- ❑ Submit CVs for all Investigators
- ❑ Submit medical licenses for all applicable members
- ❑ Execute the Clinical Trial Agreement, Investigator Agreement, and Sub-Investigator Agreement(s)
- ❑ Execute Purchasing Agreement (if not included in CTA)
- ❑ Confirm Medtronic Agreement for Valiant Captivia
- ❑ Provide signed copy of the Delegation of Authority Log
- ❑ Submit lab certification and reference ranges

Required Training

- ❑ IRB required training for research (e.g., CITI, GCP; specific to IRB)
- ❑ Study required training
- ❑ Site Initiation Visit
- ❑ EDC training
- ❑ Provide all training documentation for study team

Device Accountability

- ❑ Received 1st device shipment of 7 devices
- ❑ Completed the Investigational Device Accountability Log for 1st shipment

Keys to Site Start-Up Success

The following are considerations for a successful start-up:

- Follow-up with your PI and Artivion PM regularly
- Ask your PI to step in to facilitate when challenges arise
- Schedule SIV as soon as your site has 1 or 2 of the main deliverables (Budget, Contract, IRB approval) completed and, if needed, it can be rescheduled
- Plan to have as many of your sub-investigators as possible at your SIV
- If you ever want information on your site's status reach out to your Artivion PM or our group e-mail: ARTIZEN@artivion.com
  - For US sites, the Artivion PMs are Casey Jacketta and Alecia Charles
  - CRA's will initiate communication once the site gets closer to SIV

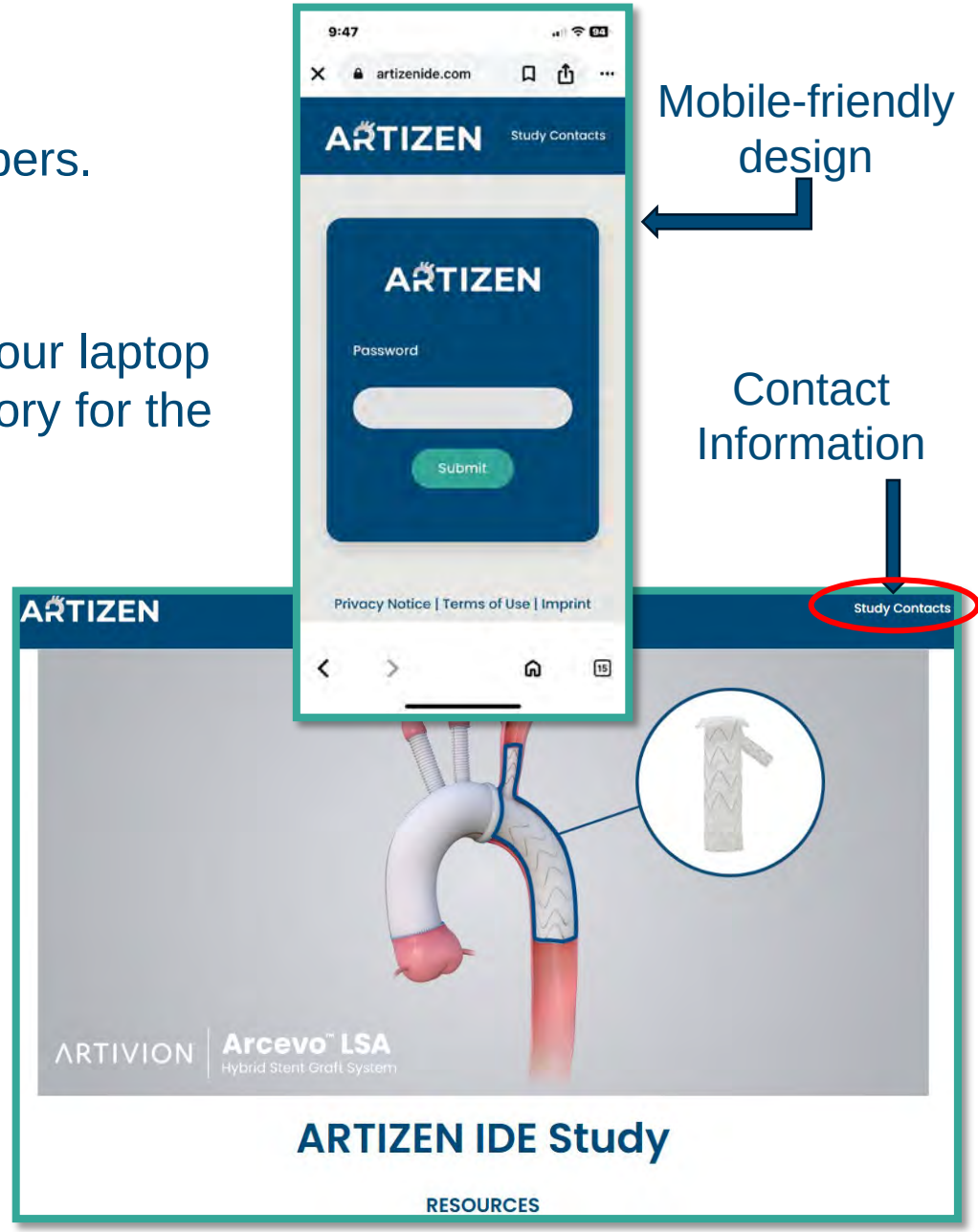
Site Start-Up Communication

- Once all deliverables are completed, the site PI and the study staff will receive an e-mail notification that your site is activated from your assigned Artivion CRA
- Only investigators listed in the e-mail will be considered active on the study
  - For any sub-investigator who is not listed on the initial activation e-mail, all remaining deliverables must be completed before the individual can participate in any study-related activity
  - Any investigator activations (after initial site activation) will also be done via e-mail
- After a site is activated, screening can begin
- Remember to setup time to meet with your Therapy Manager (i.e., Don) to review the case details prior to the scheduled surgery
- Site staff will be keeping track of all pre-screened and screened (i.e., informed consent completed) patients
  - Pre-screen failures are anyone with the intended disease, who will be treated with an open total arch replacement procedure at your institution, who has an obvious exclusion
  - Please make sure your site has a process for communicating pre-screens to coordinators

Resources & Communications After Activation

ARTIZEN Study Website

- There is a study website which is available on for study members.
  - URL: https://artizenide.com
  - Password: ARTI2025
- The website can be accessed and easily navigated through your laptop or mobile device and it serves as an easily accessible repository for the following:
  - Implantation Support
  - Sizing Sheet
  - Deployment Quick Reference Sheet
  - Instructions for Use (IFU)
  - Arcevo LSA Device Prep Guide
  - Product Animation
  - Screening Info
  - Inclusion/Exclusion Criteria
  - Forms (mRS, NIHSS, SF-12)
  - Newsletters
  - Meeting Recordings
  - Publications & Presentations
- We are currently working on populating all resources on the website and should be done soon.

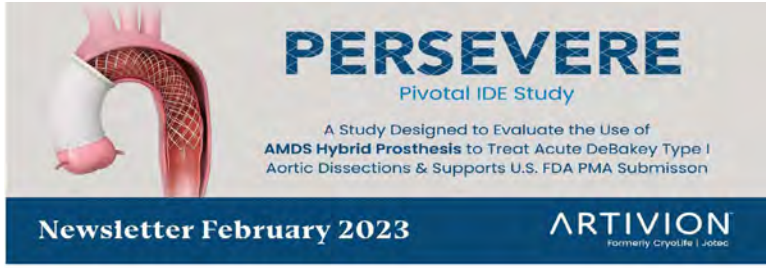


ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

ARTIZEN Study Newsletters

- Study newsletters will be sent to all site team members to communicate overall study status and to provide helpful study-related information such as:
  - Site activation updates
  - Enrollment updates (by site and overall)
  - Site achievements
  - Resources available
  - Press releases/available data
  - Hot topics
- Save newsletters in your site's regulatory binder
- Cadence will be monthly through enrollment, then quarterly
- Sent via email – make sure you provide the most current e-mails to your Artivion PM
- If you want to see any other information, just let us know

Example Newsletter Content:



Introduction

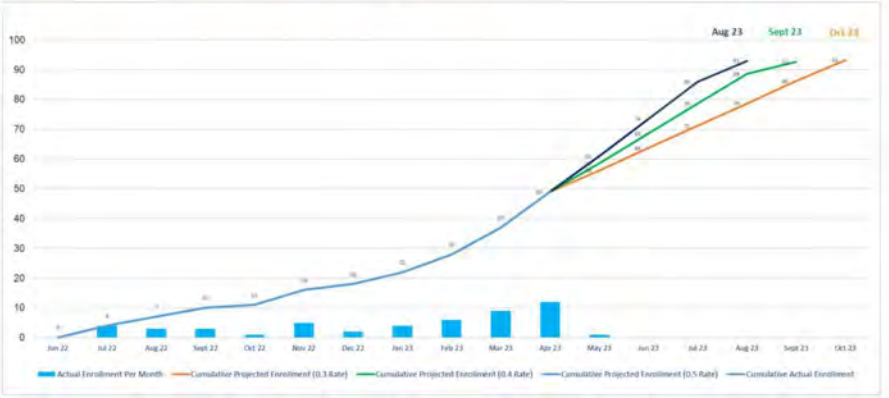
Greetings PERSEVERE Sites! We are excited to share our 7th PERSEVERE newsletter, which will cover all study activity through **January of 2023**. Happy new year to you all and thank you for your continued efforts during study start-up and enrollment.

Screening Update

- **Pre-screen Failures:** 340 patients
- **Screen Failures:** 17 patients

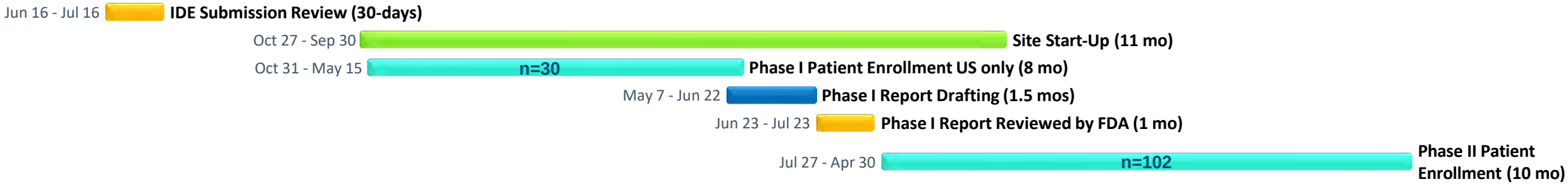
Order	Top 10 Reasons for Exclusion	#	%
1	Primary entry tear in arch or distal to LSA	61	17%
2	Diagnosis was not Acute DeBakey Type I Dissection	57	16%
3	No Malperfusion	55	15%
4	Need for total arch replacement	44	12%
5	≥ 80 years old	17	5%
6	Circulatory Shock	11	3%
7	End stage chronic kidney disease	10	3%
8	Required CPR	9	3%
9	Connective Tissue Disorder	9	3%
10	Coronary Malperfusion	8	2%

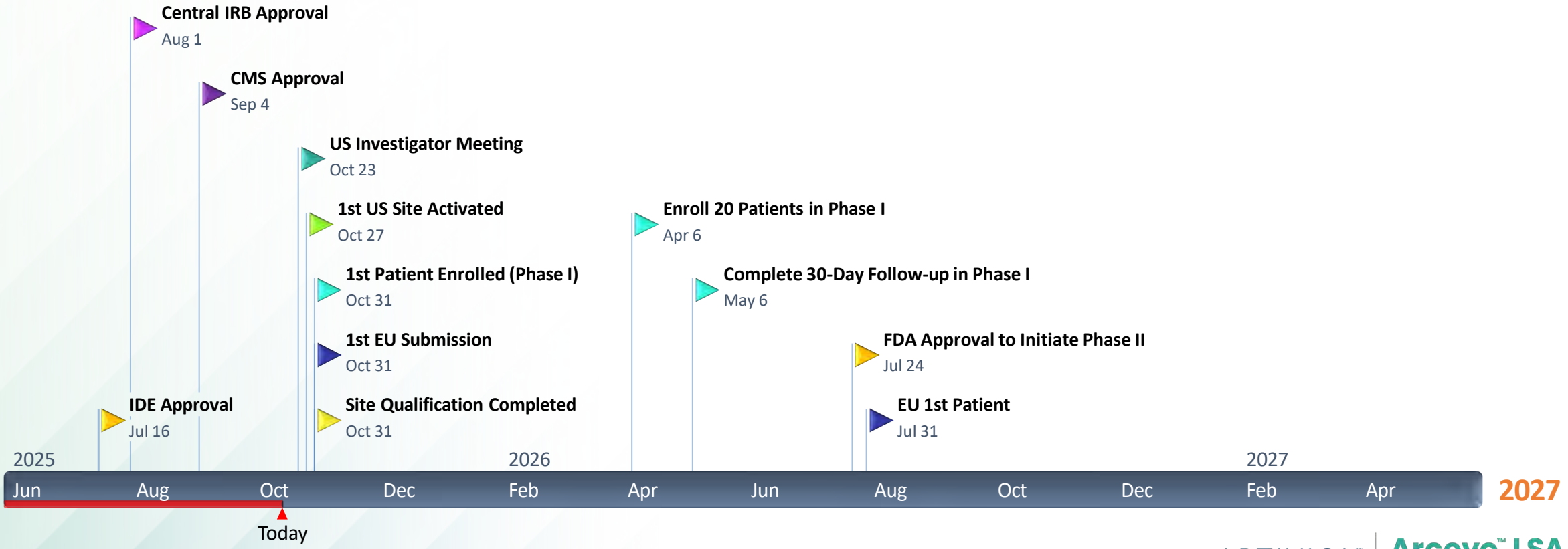
Enrollment Actuals and Projections



Timeline Review

ARTIZEN Timeline (Through Enrollment)





ARTIVION | Arcevo™ LSA Hybrid Stent Graft System

Planned Analyses

Planned Analyses

- **The following details outline our planned analyses, which will require site action to complete data entry, resolve queries, participate in IMVs, and ensure PI sign off**
- **To support major study milestones**:
  - The 1st planned analysis will occur once the first 20 consecutive patients complete 30-day follow-up and/or experience ≥1 primary major adverse event (MAE)
    - FDA will review this data to determine if we can move on to Phase II
  - The 2nd planned analysis will occur once all patients in the primary arm complete 1-year follow-up (or early terminate if <1 year) AND ≥23 (20%) patients have completed a TEVAR procedure and have a minimum of 3 months follow-up after the TEVAR.
- **To support DSMB meetings and Annual Reporting**:
  - Additional analyses are scheduled to occur to support annual reporting requirements to regulatory authorities and regularly occurring Data Safety Monitoring Board (DSMB) meetings (2x/per year).
- **Final study report:**
  - A final study report will be completed after the final patient completes their 5-year follow-up visit
  - Assuming all enrollment projections are correct, the report would be final in Q4 2032

Closing Remarks

ARTIVION™ | Arcevo™ LSA
Hybrid Stent Graft System

Questions?

Thank You!