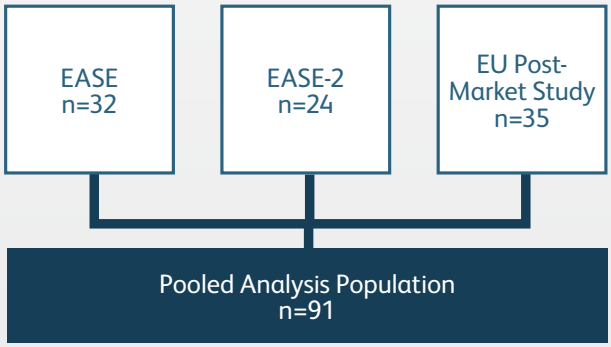
Global Data Analysis

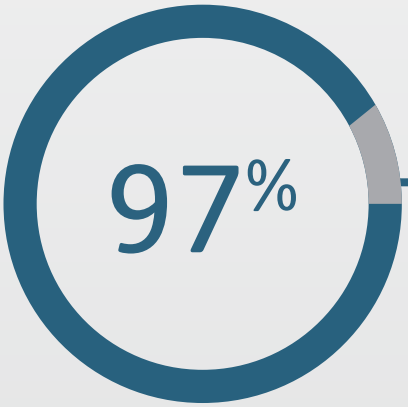
Objective: To aggregate and analyze safety and performance data from the EASE, EASE-2 and EU Study where subjects were treated with the WAVELINQ™ 4F EndoAVF System.

Analysis Design

- Data pooled in November 2018 from 7 sites across 3 studies within Germany, United Kingdom, and Paraguay.
- Enrolled subjects had chronic kidney disease and were in need of hemodialysis (including pre-dialysis patients) and were anatomically suitable for endoAVF creation.

See the WAVELINQ™ 4F EndoAVF System Instructions for Use for more details on the design of the global analysis along with the specific details of each of the studies included in the analysis.

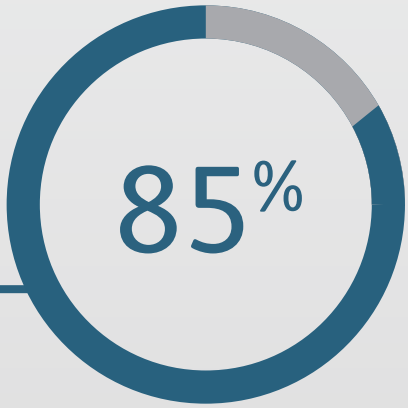




Procedure Success
n=91

Procedure Success: Successful endoAVF creation confirmed via intraprocedural fistulography or by duplex ultrasound performed post-procedure

Cannulation Success (Dialysis Subset): Successful 2-needle cannulation and dialysis through the endoAVF



2-Needle Cannulation Success
at 6 months
n=74*

WavelinQ™
EndoAVF System

*Includes subjects who were enrolled on hemodialysis or initiated hemodialysis at any point in the follow up.

BD data on file. Clinical Study Report

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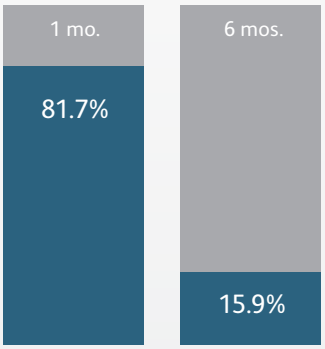
Usability

CVC Initiation & Exposure

In pre-dialysis patients, only **16%** (4/25) initiated dialysis with a CVC through 6 months



In dialysis patients, CVC exposure dropped from 81.7% (49/60) at 1 month to **15.9%** (7/44) at 6 months

	Pooled Studies
Median Time to Cannulation, Months	1.5 [IQR 1.1,2.0]
Mean Time to Cannulation, Months	2.0 (±1.6)

Time To Canulation: The time between the index procedure to the first successful endoAVF cannulation. Cannulation Success was defined as successful 2-needle cannulation and dialysis through the endoAVF.

Reintervention	Effectiveness (n = 91)
Therapeutic embolization (Coiling)	5
Balloon angioplasty	10
Stent	2
Thrombectomy and Thrombolytic Therapy	4
Transposition	5
Surgical AVF/AVG	6
Other	1
Total Interventions	33
% of patients with 0 interventions	78%

Interventions: Secondary procedures performed after the index procedure.

78%

of patients were intervention-free at 6 months post-procedure

Safety

Significant Event Summary† Safety n=91	
Device-Related Serious Adverse Event	3.3%
Procedure-Related Serious Adverse Event	5.5%
Closure-Related Adverse Event	0.0%
Coil-Related Adverse Event	0.0%

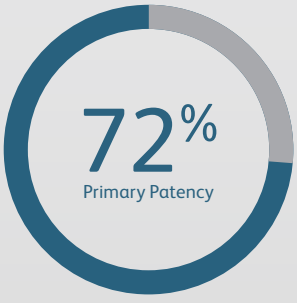
Adverse events were site-reported and reviewed by an independent Medical Monitor and the Clinical Events Committee.
† Significant Event was defined as device or procedure-related adverse events that either a) could be limb-threatening if not promptly identified or treated, or b) required additional therapy to reestablish patency of the endoAVF access circuit; irrespective of whether the event was an SAE. The independent Medical Monitor classified Significant Events based on this definition.

Definitions

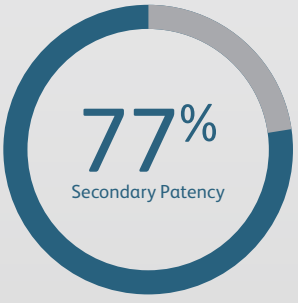
Principal Safety Endpoints (N=91)		
Endpoints	**n (%)**	**Definition**
Significant Event	20 (22.0%)[1]	Device or procedure-related adverse events that either a) could be limb-threatening if not promptly identified or treated, or b) required additional therapy to reestablish patency of the EndoAVF access circuit; irrespective of whether the event was an SAE.
Serious Adverse Event (SAE)	24 (26.4%)[2]	An event that results in the following: led to death; or led to serious deterioration in the health of the subject, that either resulted in: a life-threatening illness or injury; a permanent impairment of a body structure or a body function; in-patient or prolonged existing hospitalization; medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or body function; or led to fetal distress, fetal death or a congenital abnormality or birth defect.
Device-related SAE	3 (3.3%)[3]	Related to study device
Procedure-related SAE	5 (5.5%)[4]	Occurred during index procedure
Closure-related SAE	0 (0.0%)	Related to artery closure
Coil-related SAE	0 (0.0%)	Related to either migration of a coil from its intended site of deployment or events that are related to the obstruction of venous outflow from coil embolization; e.g. sever forearm edema associated with coil occlusion of major venous outflow channel.

Performance

Patency Rates at 6 months (Kaplan-Meier Estimates)



Primary Patency: The interval of time of access placement until any intervention designed to maintain or re-establish patency, access thrombosis, access abandonment, or the time of measurement of patency.



Secondary Patency: The interval of time of access placement until access abandonment, lost to thrombosis, or the time of patency measurement including intervening manipulations (surgical or endovascular interventions) designed to re-establish functionality in thrombosed access.

Adverse events were site-reported and reviewed by an independent Medical Monitor and the Clinical Events Committee.

[1] Included stenosis, occlusion, thrombosis and pseudoaneurysm of the access circuit and/or EndoAVF, as well as one subject with abandonment of the EndoAVF after a cannulation induced brachial artery injury

[2] Of these, 18/24 (75.0%) were unrelated to the device and unrelated to the procedure and included 6 unrelated deaths, 3 unrelated infections, 3 access circuit stenoses, 2 access circuit thromboses, 1 access circuit false aneurysm, 1 thrombosis, 1 stenosis, and 1 myocardial infarction.

[3] Included 1 thrombosis, 1 stenosis, and 1 access circuit false aneurysm.

[4] Included 2 stenoses, 1 access circuit hematoma, 1 access circuit false aneurysm, and 1 thrombosis

Characteristic	Pooled (n=91)
Sex	
Male	76 (83.5%)
Female	15 (16.5%)
Age	
Years (Mean)	54.1 ±14.7
Race*	
Caucasian	24 (26.4%)
Black	0 (0.0%)
Asian	4 (4.4%)
Indian	4 (4.4%)
Other	1 (1.1%)
Not Reported	58 (63.7%)
Ethnicity	
Not Hispanic or Latino	35 (38.5%)
Hispanic or Latino	56 (61.5%)

Characteristic	Pooled (n=91)
Body Mass Index	
BMI (Mean)	26.5 ±5.8
Key Comorbidities	
Diabetes	48.4%
Hypertension	86.8%
Coronary disease	17.1%
Cerebrovascular disease	2.9%
Peripheral vascular disease	0.0%
On hemodialysis at screening	
Yes	71.4%

± standard deviation
*Race was not entered in EASE or EASE-2 subjects; rather, only ethnicity was specified, and all subjects were Hispanic or Latino. The Pooled data for race comprise only EU Study subjects.

WavelinQ™
EndoAVF System

Indications: The WavelinQ™ 4F EndoAVF System is indicated for the creation of an arteriovenous fistula (AVF) using concomitant ulnar artery and ulnar vein or concomitant radial artery and radial vein in patients with minimum artery and vein diameters of 2.0 mm at the fistula creation site who have chronic kidney disease and need hemodialysis.

Contraindications: Target vessels < 2mm in diameter.

Warnings: The WavelinQ™ 4F EndoAVF System is only to be used with the approved components specified in the instructions for use (IFU). Do not attempt to substitute non-approved devices or use any component of this system with any other medical device system. Use of the system with other components may interfere with proper functioning of the device. The WavelinQ™ 4F EndoAVF System catheters are single use devices. DO NOT re-sterilize or re-use either catheter. Potential hazards of reuse include infection, device mechanical failure, or electrical failure potentially resulting in serious injury or death. The WavelinQ™ 4F EndoAVF System should not be used in patients who have known central venous stenosis or upper extremity venous occlusion on the same side as the planned AVF creation. The WavelinQ™ 4F EndoAVF System should not be used in patients who have a known allergy or reaction to any drugs/fluids used in this procedure. The WavelinQ™ 4F EndoAVF System should not be used in patients who have known adverse reactions to moderate sedation and/or anesthesia. The safety and performance of the device via arterial wrist access has not been fully established. The incidence of vessel stenosis or occlusion that occurs in the radial and ulnar arteries after arterial wrist access has not been evaluated. Do not use the device to create an EndoAVF using arterial access via the radial or ulnar artery. The EndoAVF should only be created using brachial artery access. Use caution when performing electrosurgery in the presence of pacemakers or implantable cardioverter defibrillators. Improper use could damage insulation that may result in injury to the patient or operating room personnel. Do not plug device into the electrosurgical pencil with ESU powered on. Consult the ESU User Guide on its proper operation prior to use. Do not use closure devices not indicated to close the artery used for access. Ensure the patient's arm is restrained to minimize movement during device activation; potential hazards of patient arm movement during activation are hematoma or pseudoaneurysm near the fistula site. The puncture site should be closed and hemostasis should be achieved by manual compression per the instructions in the IFU. Use of closure devices with the WavelinQ™ 4F EndoAVF System may be associated with an increased risk of access site complications. The WavelinQ™ 4F EndoAVF System has only been evaluated for the creation of an AVF between the ulnar artery and concomitant ulnar vein and between the radial artery and concomitant radial vein in the clinical studies described in the IFU. According to the National Kidney Foundation Kidney Disease Outcomes Quality Initiative (NKF KDOQI clinical guidelines), the device should not be used in place of a more distal AVF. This device is coated with a hydrophilic coating at the distal end of the device for a length of 23.9 cm (9.4 in). Please refer to the AVF Creation section in the instructions for use for further information on how to prepare and use this device to ensure it performs as intended. Failure to abide by the warnings in this labeling might result in damage to the device coating.

Cautions: Only physicians trained and experienced in endovascular techniques, who have received appropriate training with the device, should use the device. Endovascular technique training and experience should include ultrasound vessel access in the arm, guidewire navigation, radiographic imaging, placement of vascular embolization devices (including embolization coils), and access hemostasis. Adhere to the universal precautions when utilizing the device.

Precautions: Care should be taken during handling of the arterial and venous catheters in patients with implantable cardiac defibrillators or cardiac pacemakers to keep the distal 3 inches of the catheters at least 2 inches from the implanted defibrillator or pacemaker. Care should be taken to avoid attempting fistula creation in a heavily calcified location of a vessel as fistula may not be adequately formed. If the device does not perform properly during the creation of the endovascular fistula it is possible that a fistula will not be created or there may be some vessel injury. Some patients who have veins deeper than 6mm may require superficialization per KDOQI guidelines. Ensure the patient has adequate collateral blood flow to the hand before use of the device. Prior to the procedure, ensure that the access location, access vessels, and target AVF location are of appropriate size to account for the devices during use. Oversizing the device to the access vessel may increase risk of vessel injury, which may result in stenosis and/or occlusion. Vessel injury may impact future dialysis access options and/or the ability to perform future endovascular procedures from the target access vessels. Users should consider the potential risk of distal arterial stenosis and/or occlusion on end stage renal disease patients when selecting vascular access sites for the procedure. Adjunctive procedures are expected to be required at the time of the index procedure to increase and direct blood flow into the AVF target outflow vein to assist maturation. Care should be taken to proactively plan for any adjunctive procedures, such as embolization coil placement, when using the device.

Potential Adverse Events: The known potential risks related to the WavelinQ™ 4F EndoAVF System device and procedure, a standard AVF, and endovascular procedures may include but are not limited to: aborted or longer procedure; additional procedures; bleeding, hematoma or hemorrhage; bruising; burns; death; electrocution; embolism; failure to mature; fever; increased risk of congestive heart failure; infection; numbness, tingling and/or coolness; occlusion/stenosis; problem due to sedation or anesthesia; pseudoaneurysm; sepsis; steal or ischemia; swelling, irritation, or pain; thrombosis; toxic or allergic reaction; venous hypertension (arm swelling); vessel, nerve, or AVF damage or rupture; wound problem.

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