FLUENCY® PLUS

Endovascular Stent Graft

Instructions For Use

BARD | PERIPHERAL VASCULAR

B05667 Rev.4/05-14

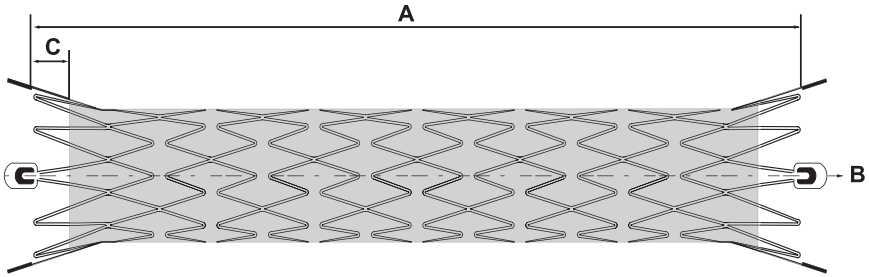
INFORMATION FOR USE

Caution: Federal law (U.S.) restricts the use of this device to sale by or on the order of a physician.

Device Description

The **Fluency® Plus Endovascular Stent Graft** implant (Figure 1) is a flexible, self-expanding vascular prosthesis **(A)** comprised of expanded polytetrafluoroethylene (ePTFE) encapsulating a Nitinol stent framework, except the flared stent graft ends with the four radiopaque Tantalum markers **(B)**. The inner lumen of the stent graft surface (blood contacting surface) is carbon impregnated. The length of the uncovered portion of the stent graft is approximately 2 mm at each end **(C)**.

Figure 1: Implant



The **Fluency® Plus Endovascular Stent Graft** is available in diameters 6 mm, 7 mm, 8 mm, 9 mm, 10 mm, 12 mm and 13.5 mm and in lengths of 40 mm, 60 mm, 80 mm, 100 mm and 120 mm.

Endovascular System (Figure 2)

The stent graft **(A)** is supplied premounted between the inner catheter **(D)** and the outer sheath **(E)** on the distal end of the endovascular system. In this compressed configuration, the Nitinol stent struts lie close together and the radiopaque markers appear as a contiguous band at each end of the stent graft.

The endovascular system is a coaxial catheter system consisting of an inner catheter **(D)**, which connects to the handgrip **(F)** via a metal tube and an outer sheath **(E)**, which connects to a Y-injection-adapter **(G)** with a Tuohy-Borst valve **(H)**.

The endovascular system has two female Luer-lock ports: one **(K)** at the proximal end of the handgrip, and the second **(L)** on top of the Y-injection-adapter.

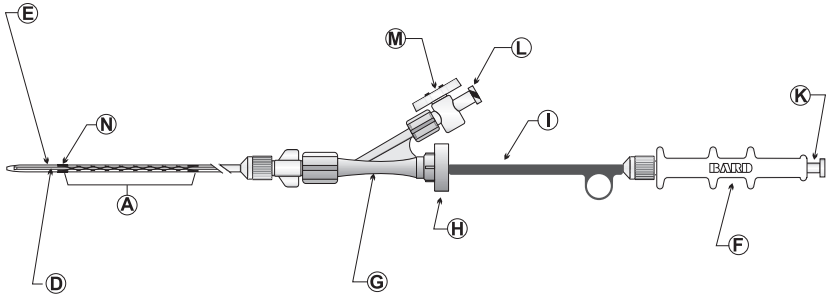
Prior to loading the endovascular system over a guide wire, both ports must be flushed with sterile saline to eliminate any air bubbles that may be trapped in the inner catheter lumen and/or the stent graft lumen. Flushing these lumens will also facilitate stent graft deployment. When flushing the stent graft lumen via the top port, ensure that the 2-way stopcock **(M)** is open, and that the Tuohy-Borst valve is closed.

Tightening the Tuohy-Borst valve (by turning it clockwise) prevents movement of the outer sheath relative to the inner catheter. There is also a removable safety clip **(I)** that prevents premature outer sheath retraction. The safety clip can be removed by pressing down on the top of the clip above the finger hole. In order to deploy the stent graft, the Tuohy-Borst valve must be open and the safety clip must be removed.

There is a radiopaque marker band **(N)** on the outer sheath of the endovascular system. Before stent graft deployment, this marker band overlaps with the radiopaque markers on the distal stent graft end. During stent graft deployment the marker band on the outer sheath will retract (towards the handgrip). When the moving marker band is past the proximal stent graft end by approximately 10 mm, the stent graft is fully released. The radiopaque markers on the proximal (inflow) end of the stent graft will have visually separated when the stent graft is released.

The **Fluency® Plus Endovascular Stent Graft** System is available in working lengths of 80 cm and 117 cm and it is compatible with 0.035" guidewires.

Figure 2: Itemized Drawing of the Fluency® Plus Endovascular Stent Graft System



LEGEND for Figures 1 & 2

Reference	Corresponding Information
A	Fluency® Plus Endovascular Stent Graft
B	Tantalum markers
C	Uncovered portion of stent graft
D	Inner catheter
E	Co-axial outer sheath
F	Handgrip
G	Y-injection-adapter
H	Tuohy-Borst valve
I	Removable safety clip
J	Intentionally left blank in IFU
K	Endovascular system female Luer port on proximal end of handgrip
L	Endovascular system female Luer port top of the Y-injection adapter
M	2-way stopcock
N	Radiopaque marker band

How Supplied:

The **Fluency® Plus Endovascular Stent Graft** is supplied sterile (by ethylene oxide gas). For single use only.

Indications for Use:

The **Fluency® Plus Endovascular Stent Graft** is indicated for use in the treatment of in-stent restenosis in the venous outflow of hemodialysis patients dialyzing by either an arteriovenous (AV) fistula or AV graft.

Contraindications:

There are no known contraindications for the **Fluency® Plus Endovascular Stent Graft**.

Warnings:

- **This device should only be used by physicians who are familiar with the complications, side effects, and hazards commonly associated with dialysis access shunt revisions and endovascular procedures.**
- **Do not expose the stent graft to temperatures higher than 500 °F (260 °C). ePTFE decomposes at elevated temperatures, producing highly toxic decomposition products.**
- **Examine the packaging and endovascular system to determine if there is any damage, defects or if the sterile barrier is compromised. Do not use the device if any of these conditions are observed.**
- **Do not resterilize. After resterilization, the sterility of the product is not guaranteed because of an indeterminable degree of potential pyrogenic or microbial contamination which may lead to infectious complications. Cleaning, reprocessing and/or resterilization of the present medical device increases the probability that the device will malfunction due to potential adverse effects on components that are influenced by thermal and/or mechanical changes.**
- **Do not reuse. This device has been designed for single use only. Reusing this medical device bears the risk of cross-patient contamination as medical devices, particularly those with long and small lumina, joints, and/or crevices between components are difficult or impossible to clean once body fluids or tissues with potential pyrogenic or microbial contamination have had contact with the medical device for an indeterminate period of time. The residue of biological material can promote the contamination of the device with pyrogens or microorganisms which may lead to infectious complications.**

- **Do not use in patients with uncorrectable coagulation disorders.**
- **Do not use in patients with bacteremia or septicemia.**
- **Do not use in patients that cannot be adequately premedicated and have a known allergy or sensitivity to contrast media.**
- **Do not use in patients with known hypersensitivity to nickel-titanium.**
- **Do not use in patients whose AV access graft/fistula is infected.**
- **Do not use in patients with an AV access graft that has been implanted for less than 30 days.**
- **Do not use in patients with an immature AV fistula.**
- **Do not use the device in patients where full expansion of an appropriately sized angioplasty balloon could not be achieved during pre-dilation.**
- **Use the device prior to the USE BY date specified on the package.**
- **Do not use if packaging/pouch is damaged.**
- **Do not use the device if the endovascular system cannot be flushed prior to use. Flushing is required prior to insertion or reinsertion.**
- **The delivery catheter is not intended for any use other than stent graft deployment.**
- **Placing a stent graft across a vessel side branch may impede blood flow and hinder or prevent future procedures.**
- **The stent graft (implant) cannot be repositioned within the vessel after total or partial deployment.**
- **Once partially or fully deployed, the stent graft cannot be retracted or remounted onto the delivery system.**
- **Do not attempt to move the implant during or after deployment as this may cause interaction with the bare metal stent.**
- **The effects of direct cannulation on the stent graft have not been evaluated in a clinical study.**
- **Notify the patient that the stent graft should not be cannulated and applying pressure to the implant area should be avoided.**

Precautions:

- Prior to stent graft deployment, refer to the Stent Graft Sizing Table (Table 1) and read the Instructions for Use.
- Faulty placement techniques may lead to stent graft deployment failure.
- A 0.035" guidewire is required for the introduction of the endovascular system. The guidewire must remain in place during the introduction, manipulation and removal of the endovascular system.
- Careful attention should be paid to ensure the device is appropriately sized to the achievable lumen, taking into account any change to the stated treatment area diameter that may have resulted from previous interventions. Under-sizing the device may result in device migration.
- The appropriate length device(s) should be selected so that the stent graft extends at least 10 mm distally (outflow) and 10 mm proximally (inflow) beyond the lesion into the non-diseased vessel.
- The safety and effectiveness of the device when placed across a tight bend including the terminal cephalic arch or across the elbow joint has not been evaluated.
- The safety and effectiveness of the device when placed across an aneurysm or a pseudaneurysm has not been evaluated.
- The safety and effectiveness of the device when used in the Superior Vena Cava has not been evaluated.
- The safety and effectiveness of the device when placed across a fractured bare metal stent has not been evaluated.
- The device has not been tested for use when used around a tight bend such as an AV loop graft.
- The device has not been tested for use in an overlapped condition with another Fluency® Plus Stent Graft.
- Do not kink the delivery catheter or use excessive force during delivery to the target lesion.
- Post dilation of the stent graft must be performed with a PTA balloon catheter no larger than the previously placed bare metal stent.
- The stent graft implant cannot be expanded with an angioplasty balloon beyond its stated diameter.
- Ensure that the Tuohy-Borst valve on the Y-injection-adapter is closed during insertion and manipulation of the endovascular system.
- Prior to stent graft deployment, ensure that the proximal (inflow) stent graft end is positioned in a straight section of the lumen to reduce the risk of higher deployment forces and possible endovascular system failure.
- The endovascular system will function after the safety clip is removed and the Tuohy-Borst valve is loosened. This should not be undertaken until the stent graft is at the target location and ready to be deployed.
- Higher deployment force may be encountered with longer length stent grafts.
- If unusual resistance or high deployment force is encountered during stent graft deployment, abort the procedure, remove the delivery system and use an alternative device.
- If resistance is encountered when removing the delivery system, it is recommended to remove the delivery system, introducer and guidewire as a single unit.
- Careful attention of the operator is warranted to mitigate the possibility of distal (central venous system) migration of the stent graft during deployment. After deployment of approximately15 mm of the stent graft, wait for the distal end the stent graft to fully expand.

- When passing a PTA balloon catheter through the deployed stent graft for post dilation, advance the PTA balloon catheter under fluoroscopy to ensure that the stent graft is not dislodged.
- Do not attempt to re-sheath the delivery system after stent graft release.
- Clinical investigations regarding the safety and effectiveness of the device have been limited to implants placed within AV grafts/fistula located in the upper extremities.

Potential Complications:
Complications and Adverse Events associated with use of the **Fluency® Plus Endovascular Stent Graft** may include the usual complications associated with endovascular stent and stent graft placement and dialysis shunt revisions. These may include the following: Allergic reaction, aneurysm, arm or hand edema, bleeding at access site, blood leakage from delivery system (hemostasis), bond joint failures, cellulitis, cerebrovascular accident, congestive heart failure, death, delivery system kinking, detachment of part, face or neck edema, failure to deploy, fever, hematoma, hemoptysis, hemorrhage, high deployment forces, inability to track to target location, inaccurate deployment, incompatibility with accessory devices, infection, insufficient stent graft expansion, no visibility under fluoroscopy, pain, perforation, premature deployment, prolonged bleeding, pseudoaneurysm, rash, reaction to contrast, restenosis requiring reintervention, sepsis, steal syndrome, stent graft embolism, stent graft fracture, stent graft kinking, stent graft migration, stent graft misplacement, thrombotic occlusion, ventricular fibrillation, or vessel rupture.

The above complications may be associated with adverse events, medical or surgical intervention and/or death.

MR Conditional Information:
Non-clinical testing and analysis has demonstrated that the **Fluency® Plus Endovascular Stent Graft** in combination with a bare metal stent is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5-Tesla or 3-Tesla.
- Spatial gradient field of 2500 Gauss/cm (25 T/m) or less.
- Maximum whole-body-averaged specific absorption rate (SAR) of 1 W/kg for 15 minutes of scanning for stent graft placement in the arms. For stent graft placement in the torso, the whole body SAR may be 2 W/kg for 15 minutes of scanning.
- In a configuration where the patients arms are not in contact with each other or touching the body.
- Normal mode operation of the MR system.
- A radiofrequency (RF) head transmit coil may be used. The safety of other MR local coils has not been evaluated.

Summary of Nonclinical Tests:
3 Tesla (128 MHz). Temperature rises of the **Fluency® Plus Endovascular Stent Grafts** in combination with bare metal stents were measured in a nonclinical configuration according to ASTM F2182-09 using a GE Signa HDX whole body active shield MR scanner using software version 14/ LX/MR and a phantom designed to simulate human tissue. The maximum temperature rise after 15 minutes of scanning was 1.4 °C when scaled to a local background SAR of 1 W/kg. This rise was measured for a configuration with a 6 x 80 mm **Fluency® Plus Endovascular Stent Graft** overlapped by a 6 x 60 mm bare metal stent. Other configuration tested yielded a lower temperature rise. An analysis based on measured temperature rises and the electric fields in the body during MRI yielded a maximum projected in-vivo rise of 4.9 °C. This rise is conservative because blood flow and perfusion in the tissues surrounding the stent were not considered.

1.5 Tesla (64 MHz). Temperature rises of **Fluency® Plus Endovascular Stent Graft** in combination with bare metal stents were measured in a nonclinical configuration according to ASTM F2182-09 using a GE Signa whole body coil and a phantom designed to simulate human tissue. The maximum temperature rise after 15 minutes of power application was 3.8 °C when scaled to a local background SAR of 2W/kg. This rise was measured for a configuration with a 6 x 120 mm **Fluency® Plus Endovascular Stent Graft** overlapped by a 6 x 100 mm bare metal stent. Other configurations tested yielded a lower temperature rise. An analysis based on measured temperature rises and the electric fields in the body during MRI yielded a maximum projected in-vivo rise of 6.5 °C. This rise is conservative because blood flow and perfusion in the tissues surrounding the stent were not considered.

Image distortion was evaluated according to ASTM F2119 in the same GE Signa HDx MR system used for the 3T heating tests. Distortion beyond the **Fluency® Plus Endovascular Stent Graft** was about 5 mm for the spin echo sequence and 8 mm for the gradient echo sequence. The lumen of **Fluency® Plus Endovascular Stent Graft** and the bare metal stent were partially obscured. It may be necessary to optimize MR imaging parameters for the presence of this metallic implant.

Magnetic force was measured with the deflection technique of ASTM F2052 in the GE Signa HDX MR system. The deflection angle was less than 2° at the edge of the bore of the scanner, where the spatial gradient was 4.7 T/m and the static field intensity was 1.7 T.

NOTE: The effect of heating in the MRI environment for stent grafts with fractured struts is not known.

Storage:
Store in a cool, dry place. Keep away from sunlight. Use by the end of the month indicated by the "Use By" date specified on the package.

Disposal Instructions:
After use, this product may be a potential biohazard. Handle and dispose of in accordance with accepted medical practice and applicable local, state and federal laws and regulations.

Stent Graft Sizing and Selection:

Special care must be taken to ensure that the appropriate size **Fluency® Plus Endovascular Stent Graft** is selected prior to introduction.

In order to ensure sufficient wall apposition, it is recommended to oversize the stent graft relative to the healthy (non-diseased) portion of the vessel.

Table 1: Stent Graft Sizing and Selection Table

Reference Vessel Diameter*	Recommended Stent Graft Diameter	Stent Graft Oversizing
5.0 mm – 5.5 mm	6 mm	0.5 mm – 1.0 mm
5.0 mm – 6.0 mm	7 mm	1.0 mm – 2.0 mm
6.0 mm – 7.0 mm	8 mm	1.0 mm – 2.0 mm
7.0 mm – 8.0 mm	9 mm	1.0 mm – 2.0 mm
8.0 mm – 9.0 mm	10 mm	1.0 mm – 2.0 mm
9.0 mm – 11.0 mm	12 mm	1.0 mm – 3.0 mm
11.0 mm – 12.0 mm	13.5 mm	1.5 mm – 2.5 mm

*The largest diameter (post balloon angioplasty) of the healthy vessel segment adjacent to the lesion.

NOTE:

- **In order to ensure safe stent graft placement and lesion coverage, it is recommended that the stent graft extends a minimum of 10 mm distally (outflow) and 10 mm proximally (inflow) beyond the lesion at both ends.**
- **If a stent graft is oversized per Table 1, there will be minimal foreshortening (<10%) of the stent graft during deployment.**
- **Keep in mind that approximately 2 mm of each stent graft end is uncovered.**

Materials required for the Fluency® Plus Endovascular Stent Graft Procedure:

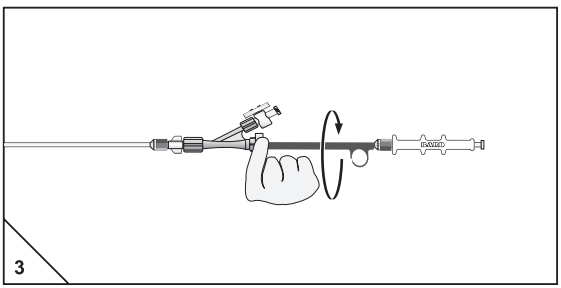
- Heparinized saline
- Sterile syringes
- 0.035" (0.889 mm) guidewire with a length at least twice as long as the endovascular system
- Introducer sheath with appropriate inner diameter
- Balloon angioplasty catheter for pre and/or post dilation
- Inflation device
- Diagnostic catheters and accessories
- Contrast Medium

DIRECTIONS FOR USE

Preparation:

1. Carefully remove the endovascular system from its packaging and inspect packaging and system for any damage or defects. Do not use if the sterile barrier is compromised.
2. The use of an appropriately sized introducer sheath is recommended.
3. Prepare a stiff 0.035" guidewire per its Instructions for Use and advance the guidewire under fluoroscopy to the target location.
4. Select an appropriate stent graft diameter and stent graft length based on the Stent Graft Sizing and Selection Table listed above (Table 1).
5. Pre dilate the stented restenotic lumen with a balloon diameter no larger than the previously placed bare metal stent.
6. Remove the endovascular system from the packaging and tighten the Tuohy-Borst valve on the Y-injection-adapter by turning it clockwise. (see figure 3)

Figure 3

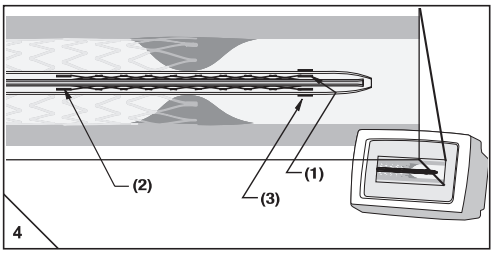


7. Flush the stent graft lumen with sterile saline by using a small volume syringe.
   a) Attach the syringe to the Luer port at the back of the endovascular system and flush the endovascular system until saline leaks from the distal tip of the catheter.
   b) Attach the syringe to the Luer port on the Y-adapter, open 2 way stopcock (in line with Y-adapter) and flush the endovascular system until saline leaks from the distal end of the endovascular system. Close the stopcock when flushing is complete and remove the syringe from the Luer port.

Introduction of the endovascular system:

8. Under radiographic guidance, advance the stent graft across the lesion. Use the radiopaque stent graft ends to center the stent graft. It is recommended to advance the endovascular system past the lesion and then pull back slightly on the entire system to attain correct positioning of the radiopaque markers and ensure slack is removed from the endovascular system.
9. Ensure the delivery catheter is straight and the stent graft extends a minimum of 10 mm distally (outflow) and 10 mm proximally (inflow) beyond the lesion into the non-diseased vessel.
10. Confirm the position of the radiopaque markers on the stent graft ends (see figure 4). It is recommended that the position of the stent graft ends (1, 3) and (2) should be marked on the screen.

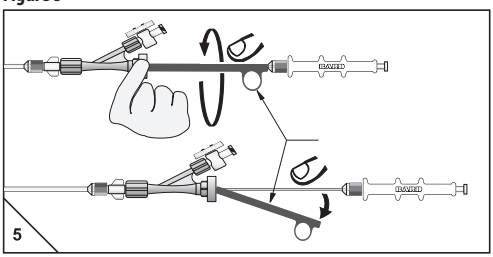
Figure 4



Stent Graft Deployment:

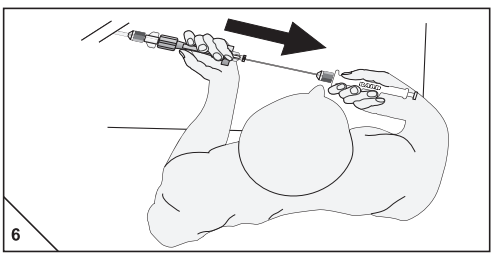
11. When the stent graft is ready for deployment, open the Tuohy-Borst valve by turning it counter clockwise and remove the safety clip by pressing down on the top of the grip surface with the thumb and pulling downward. (see figure 5).

Figure 5



12. Confirm that the stent graft position remains unchanged by examining the radiopaque markers.
13. To deploy the implant, pin the handgrip on a stable surface with your back hand and slowly pull the Y-injection-adapter with your front hand towards the handgrip. This action retracts the outer sheath and exposes a corresponding portion of the stent graft. The back hand should stay fixed in position with slight adjustments as necessary to allow for proper deployment (see figure 6).

Figure 6



14. Deploy the first 15 mm of the stent graft slowly until the distal stent graft end has expanded. Once the distal (outflow) portion has fully expanded, deploy the remainder of the stent graft slowly.

    NOTE: Higher deployment force may be encountered with longer length stent grafts or in tortuous anatomy.

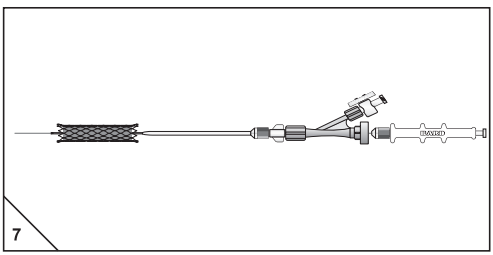
IMPORTANT:

- **When deploying the stent graft, the delivery system should be kept as straight as possible. Slight back tension on the handgrip is recommended to ensure that the delivery system is stationary and straight.**
- **Do not hold or kink the outer sheath of the delivery catheter.**
- **Ensure the Y-injection-adapter and outer sheath move during stent graft deployment and the handgrip is stationary.**
- **If unusual resistance or high deployment force is encountered during stent graft deployment, abort the procedure, remove the delivery system and use an alternative device of the same size.**

15. The stent graft is fully deployed when the Tuohy-Borst valve touches the handgrip (see figure 7).

    Additionally, the radiopaque markers on the proximal end of the stent graft will have separated once fully deployed. After full stent graft deployment, wait for complete device expansion before removing the delivery system over the guidewire.

Figure 7

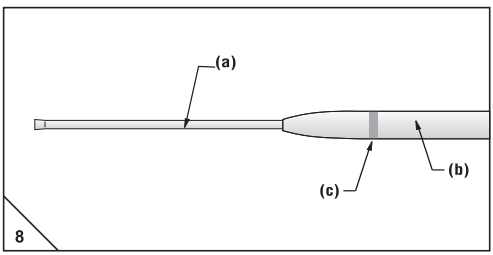


16. Remove the delivery system under fluoroscopy while maintaining guidewire access. Do not attempt to re-sheath the delivery system after the stent graft has been deployed.

    NOTE: If resistance is encountered removing the delivery system, it is recommended to remove the delivery system, introducer and guidewire as a single unit.

17. After removing the delivery system, visually confirm that the complete system has been removed. (see figure 8)
    - *(a) inner catheter with distal flared end*
    - *(b) outer sheath with radiopaque marker band (c)*

Figure 8



18. Post dilate the stent graft with an angioplasty balloon sized appropriately as to ensure complete wall apposition to the reference vessel.

19. Examine the implanted stent graft under fluoroscopy to verify final stent graft position.

Post Procedure Precaution:

The effects of direct cannulation of the **Fluency® Plus Endovascular Stent Graft** have not been determined. Notify the patient that the stent graft should not be directly cannulated and that applying pressure to the implant area should be avoided.

Patient Implant Information Card:
A Patient Implant Information Card is provided with this device. The Patient Data, Implant Data, and Hospital Data should be carefully recorded on the card and given to the patient.

Apply one of the peel-off stickers found on the product labels on the product carton box or on the pouch to the indicated area on the Patient Implant Information card. This peel-off sticker contains important information about the patient's stent graft implant. The patient should carry this card with them and provide to any medical personnel caring for the patient in the future.

SUMMARY OF CLINICAL STUDY

A total of 265 patients were treated at 23 U.S. investigational sites in this prospective, multi-center, randomized, concurrently-controlled clinical study designed to assess the safety and effectiveness of the Fluency® Plus Endovascular Stent Graft. A total of 781 subjects were screened for eligibility, while 265 subjects were randomized and treated. The primary reason for exclusion from the study was the subjects' failure to meet the target lesion angiographic specific criteria. The primary purpose of this study was to demonstrate that the Fluency® Plus Endovascular Stent Graft can effectively and safely treat in-stent restenotic lesions in the venous outflow of the AV access circuit of hemodialysis patients with either of the two predominant vascular access types – those with an AV graft and those with an AV fistula. This study compared the use of the Fluency® Plus Endovascular Stent Graft (following PTA) to PTA alone.

At the time of this interim analysis, the 265 patients randomized into the Intent-to-Treat (ITT) group were evaluated for the primary and secondary endpoints. Of this group, the ITT analyses were conducted on patients who had reached pre-specified follow-up time points. As such, evaluation of the primary safety endpoint at 30 days included 244 patients (118 in the treatment arm and 126 in the control arm), while evaluation of the primary effectiveness endpoint at six months included 220 patients (109 in the treatment arm and 111 in the control arm). Patients will be followed through 24 months.

Study Endpoints
Access Circuit Primary Patency (ACPP) at six months was the primary outcome used to compare the effectiveness of the **Fluency® Plus Endovascular Stent Graft** to the PTA Control. The primary safety endpoint was evaluated based on the incidence of safety events observed through 30 days.

Secondary endpoints included: (1) Post-Intervention Lesion Patency at 30 days, 90 days and 12 months; (2) Access Circuit Primary Patency at 30 days, 90 days, 12 months, 18 months and 24 months; (3) Index of Patency Function at 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (4) Index of Patency Function – Target Lesion at 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (5) Secondary Patency at 30 days, 90 days, 6 months, 12 months, 18 months and 24 months; (6) Binary Restenosis at 90 days; (7) Technical and Procedural Success; and (8) Safety at 90 days, 6 months, 12 months, 18 months and 24 months.

Patients studied
Eligible patients had a hemodynamically significant stenosis ≥50% and clinical evidence of AV graft or AV fistula dysfunction (without thrombotic occlusion), with angiographic evidence of a previously placed bare metal stent located in the venous outflow of the AV access circuit. To be included in the study, the target lesion must have been located in the restenosed bare metal stent extending no more than 3 cm beyond the bare metal stent end, and must have been ≤ 10 cm in length. The AV access graft must have been implanted at least 30 days, or the AV fistula located in the arm must have been mature, and must have undergone at least one successful hemodialysis session.

Patients were excluded from the study if they had a thrombosis treated within 7 days before the index procedure, or if the restenosed bare metal stent was determined by angiography to be fractured. Patients were also excluded for a variety of conditions which would make the implantation procedure more difficult or would confound the interpretation of the study results.

Methods
Patients were prospectively randomized to treatment with the **Fluency® Plus Endovascular Stent Graft** or PTA. Cross-overs were not allowed. Clinical follow-up visits were conducted at thirty and ninety days, and at six months after the index procedure. Interim visits were conducted as clinically indicated. Qualitative angiography was conducted in conjunction with the 90-day follow-up visit. Antiplatelet and anticoagulation therapy was at the discretion of the physician. Patients were monitored for adverse events throughout the trial.

An independent Clinical Events Committee (CEC) adjudicated all adverse events and serious adverse events. Additionally, an independent Data Safety Monitoring Board (DSMB) reviewed safety information including site reported events and summaries of CEC adjudication activities. The DSMB determined and made recommendations on whether the study should continue as described, or if changes should be made.

For effectiveness, the primary endpoint was measured by percentage of subjects with Access Circuit Primary Patency (ACPP) through 6 months and was estimated using the Kaplan-Meier method. The primary effectiveness endpoint comparing PTA to FLUENCY® PLUS (stratified by access type) was tested, using a stratified log rank test at a two-sided significance level of 0.05.

For safety, the non-inferiority of FLUENCY® PLUS to PTA in the primary safety endpoint was tested using a Farrington and Manning Exact Test at a one-sided significant level of 0.05.

Additionally, similar to the analysis of the primary effectiveness endpoint, the secondary effectiveness endpoint of Post-intervention Lesion Patency (PLP) was compared between FLUENCY® PLUS and PTA using a stratified log rank test at a two-sided significance level of 0.05. This test was conducted after both primary tests were successful to control for multiplicity.

Results

PATIENT DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Tables 2 - 4 summarize the patient demographics, medical history, and the AV Access circuit description.

Table 2: Patient Demographics

	PTA Alone (N=137)	FLUENCY® PLUS (N=128)	All Patients (N=265)
Age (years) [1]		**p=0.691 [2]**	
Mean (SD)	62.2 (13.55)	61.5 (13.42)	61.9 (13.47)
Min, Max	27, 93	34, 89	27, 93
Sex		**p=0.741 [3]**	
Female	67 (48.9)	60 (46.9)	127 (47.9)
Male	70 (51.1)	68 (53.1)	138 (52.1)

[1] Age is calculated as the date of informed consent minus date of birth.
[2] P value is from t test
[3] P value is from z test

Table 3: Medical History

	PTA Alone (N=137)	FLUENCY® PLUS (N=128)	All Patients (N=265)
	n (%)	**n (%)**	**n (%)**
Congestive Heart Failure	38 (27.7)	37 (28.9)	75 (28.3)
Coronary Heart Disease	42 (30.7)	52 (40.6)	94 (35.5)
Diabetes Mellitus	86 (62.8)	87 (68.0)	173 (65.3)
Hypercoagulation	3 (2.2)	1 (0.8)	4 (1.5)
Hypertension	130 (94.9)	116 (90.6)	246 (92.8)
Glomerulonephritis	4 (2.9)	5 (3.9)	9 (3.4)
Peripheral Vascular Disease	17 (12.4)	14 (10.9)	31 (11.7)
Steal Syndrome	2 (1.5)	3 (2.3)	5 (1.9)
Cerebrovascular Accident	19 (13.9)	26 (20.3)	45 (17.0)
Transient Ischemic Attack	7 (5.1)	5 (3.9)	12 (4.5)
Other Pre-Existing Conditions	133 (97.1)	127 (99.2)	260 (98.1)

Table 4: Description of the Access Circuit

	PTA Alone (N= 137)	FLUENCY® PLUS (N= 128)	All Patients (N= 265)
AV Access Type	**n (%)**	**n (%)**	**n (%)**
Graft	63 (46.0)	59 (46.1)	122 (46.0)
Mature Fistula	74 (54.0)	69 (53.9)	143 (54.0)
Location	**n (%)**	**n (%)**	**n (%)**
Right Arm	44 (32.1)	47 (36.7)	91 (34.3)
Left Arm	93 (67.9)	81 (63.3)	174 (65.7)
Position	**n (%)**	**n (%)**	**n (%)**
Forearm	17 (12.4)	21 (16.4)	38 (14.3)
Upper Arm	120 (87.6)	107 (83.6)	227 (85.7)
Time Since Implantation/Creation (Months)			
n	130	119	249
Mean (SD)	41.0 (27.09)	34.8 (23.95)	38.0 (25.77)
Min, Max	2, 154	6, 159	2, 159

TARGET LESION CHARACTERISTICS

Table 5 summarizes target lesion characteristics at baseline of the test and control groups.

Table 5: Target Lesion Characteristics at Index Procedure

	PTA Alone (N= 137)	Fluency® Plus (N= 128)	All Patients (N= 265)
Target Lesion Location	**n (%)**	**n (%)**	**n (%)**
Central Vein	52 (38.0)	41 (32.0)	93 (35.1)
Peripheral Vein	83 (60.6)	86 (67.2)	169 (63.8)
Target Lesion Length (cm)			
Mean (SD)	2.92 (1.67)	3.17 (1.80)	3.04 (1.73)
Min, Max	0.5, 8.0	0.5, 10.0	0.5, 10.0
Percentage of Stenosis (%)			
Mean (SD)	69.75 (13.87)	71.25 (13.13)	70.48 (13.51)
Min, Max	50.0, 100.0	50.0, 100.0	50.0, 100.0
Reference Vessel Diameter at the Restenosed Bare Metal Stent (mm)			
Mean (SD)	9.51 (1.97)	9.18 (1.69)	9.35 (1.85)
Min, Max	5.0, 14.5	5.0, 12.0	5.0, 14.5
Additional Stenotic Lesions in the Venous Outflow that were > 3 cm from the Edge of the Target Lesion			
Yes	78 (56.9)	65 (50.8)	143 (54.0)
No	59 (43.1)	63 (49.2)	122 (46.0)

Patient Accountability

Investigators treated 265 patients at 23 sites. Two-hundred forty-four (244) patients were included in the 30 day primary safety endpoint analysis and 220 patients in the six month primary effectiveness endpoint analysis. At the time of this interim analysis, a total of 21 patients did not yet have their 30 day follow up visit or had discontinued within 30 days without a safety event and were excluded from the safety analysis. A total of 45 active patients had not yet reached their 6 month follow up visit and were excluded from the effectiveness analysis.

Summary of Safety

The primary safety endpoint for this study was noninferiority of Fluency® Plus Endovascular Stent Graft to PTA alone for freedom from safety events through 30 days. The endpoint is defined as freedom through 30 days from any adverse event(s) (AEs), localized or systemic, which reasonably suggests the involvement of the AV access circuit (not including stenosis or thrombosis) that require or result in any of the following alone or in combination: additional interventions (including surgery); in-patient hospitalization or prolongation of an existing hospitalization; or death. Analyses are presented for safety events as adjudicated by the blinded Clinical Endpoint Committee (CEC). Tables 6 and 7 show the results of the analyses for Freedom from any Safety Events / Adverse Events through 30 days.

Table 6: Freedom from any Safety Event [1] through 30 days

	PTA Alone (n=137)	Fluency® Plus (n=128)	Non-inferiority p-value [1]
Overall Population (Primary Safety)			
n/N (%)	122/126 (96.8)	114/118 (96.6)	0.007
95% Confidence Interval	(92.07, 99.13)	(91.55, 99.07)	

[1] The p-value is based on a non-inferiority Farrington and Manning Exact Test.

Table 7: Incidence of Primary Safety Endpoint in First 30 Days

	PTA Alone (N=111)	Fluency® Plus (N=128)
Number of Patients Reporting At Least One Safety Event AE	4 (2.9)	4 (3.1)
Infection	1 (0.7)	1 (0.8)
Arm or Hand Edema	0	2 (1.6)
Vessel Rupture	1 (0.7)	0
Allergic reaction to uncertain source	0	1 (0.8)
Fever/cellulitus of both legs/sepsis	0	1 (0.8)
Ventricular fibrillation	1 (0.7)	0
Infolded covered stent	1 (0.7)	0

The percentage of patients (AV graft and fistula patients) free from safety events through 30 days was 96.8% (95% CI: 92.07, 99.13) for patients with PTA alone, and 96.6% (95% CI: 91.55, 99.07) for patients with **FLUENCY® PLUS Endovascular Stent Graft** (non-inferiority p-value = 0.007). Thus, the non-inferiority (δ = 0.075) of **FLUENCY® PLUS Endovascular Stent Graft** to PTA alone with regard to this primary safety endpoint is confirmed.

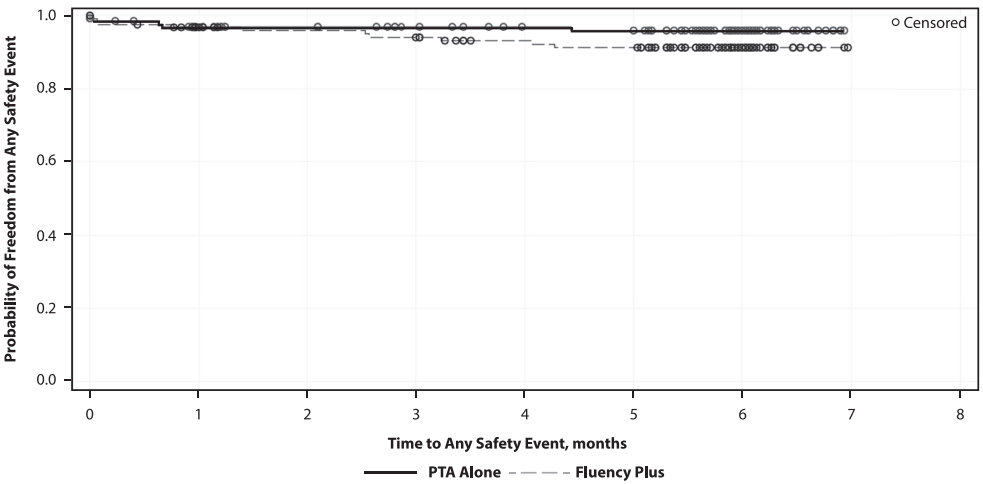
A list of Safety Events observed in the Clinical Study through six months can be found in Table 8, and a list of device and/or procedure related AEs can be found in Table 9. AEs are defined as those that reasonably suggest the involvement of the AV access circuit (not including stenosis or thrombosis). A Clinical Events Committee (CEC) and Data Safety Monitoring Board (DSMB) reviewed all AEs and safety trends. The Kaplan-Meier analysis of freedom from any safety event through 6 Month follow-up is provided in Figure 9.

Table 8: Safety Events through 6 months (Randomized Patients)

Parameter	PTA Alone (N=137)	Fluency® Plus (N=128)	Overall (N=265)
Number of Safety Events Reported	8	11	19
Number(%) of Patients Reporting Safety Events	5 (3.6)	10 (7.8)	15 (5.7)
Diagnosis/Event Name			
Hemorrhage	0	2 (1.6)	2 (0.8)
Infection	2 (1.5)	2 (1.6)	4 (1.5)
Pain	1 (0.7)	0	1 (0.4)
Arm or Hand Edema	0	2 (1.6)	2 (0.8)
Pseudoaneurysm	0	2 (1.6)	2 (0.8)
Vessel Rupture	2 (1.5)	0	2 (0.8)
Other	3 (2.2)	2 (1.6)	5 (1.9)
Other: Allergic reaction. to uncertain source; rash on right arm	0	1 (0.8)	1 (0.4)
Other: Fever/cellulitis of both legs/sepsis	0	1 (0.8)	1 (0.4)
Other: Infolded covered stent	1 (0.7)	0	1 (0.4)
Other: Prolonged Bleeding	1 (0.7)	0	1 (0.4)
Other: Ventricular Fibrillation	1 (0.7)	0	1 (0.4)
Other: Hemoptysis	0	1 (0.8)	1 (0.4)

Note: Patients with multiple events may be counted more than once (in more than one category).

Figure 9: Kaplan Meier Analysis for Freedom from Any Safety Event through 6 Month Follow-Up Visit (Randomized Patients)



The rate of freedom from any safety event through 90 days in the randomized patient population was 97.0% (95% CI: 94.09, 99.90) for PTA alone, and 94.2% (95% CI: 89.99, 98.37) for **FLUENCY® PLUS Endovascular Stent Graft**. The rate of freedom from any safety event through 6 months in the randomized patient population was 96.0% (95% CI: 92.62, 99.46) for PTA alone, and 91.3% (95% CI: 86.19, 96.49) for **FLUENCY® PLUS Endovascular Stent Graft.**

Table 9: All Device and/or Procedure Related Adverse Events through 6 months (inclusive of reported Safety Events in Table 8)

Treatment Group	Description of AE
PTA	Vessel Rupture: Right Axillary Vein
	Contrast Reaction
	Prolonged Bleeding
	Pain: Access Arm – Left Upper Arm
	Infolded Covered Stent
	Pain: Left Shoulder
	Vessel Rupture: Cephalic Vein in Left Shoulder Area
Fluency Plus	Pseudoaneurysm: Basilic Vein Adjacent To Stent
	Pseudoaneurysm: Cannulation Zone of Access
	Bilateral Face Edema
	Pain: Shoulder and Neck
	Infection (Old Stent in Fistula)
	Arm or Hand Edema (Left Arm Swelling)
	Pain: All Over Body
	Allergic Reaction to Uncertain Source (Rash on Right Arm)
	Arm or Hand Edema (Entire Left Upper Extremity)

Primary Effectiveness Results

Access Circuit Primary Patency (ACPP) at six months was the primary outcome used to compare the effectiveness of the **Fluency® Plus Endovascular Stent Graft** to the PTA Control.

ACPP was defined as the interval following placement of the FLUENCY® PLUS Endovascular Stent Graft until thrombosis or re-intervention of the AV access circuit. ACPP ended with a re-intervention anywhere within the access circuit, from the arterial inflow to the superior vena cava-right atrial junction. The primary effectiveness endpoint of ACPP through 6 months is a binary endpoint and reflects the percentage of patients who are free from thrombosis or re-intervention for at least 6 months.

The ACPP rate was significantly higher ($p<0.001$) in the **Fluency® Plus Endovascular Stent Graft** group (16.7%) than in the PTA Control (3.0%), as detailed in Table 10. Additionally, the ACPP event hazard ratio demonstrated is 0.59. The reduction in the risk of failure of ACPP events due to the use of Fluency® Plus Endovascular Stent Graft compared to PTA alone is 41%.

This demonstrated superiority of the **Fluency® Plus Endovascular Stent Graft** to the PTA Control with respect to Access Circuit Primary Patency.

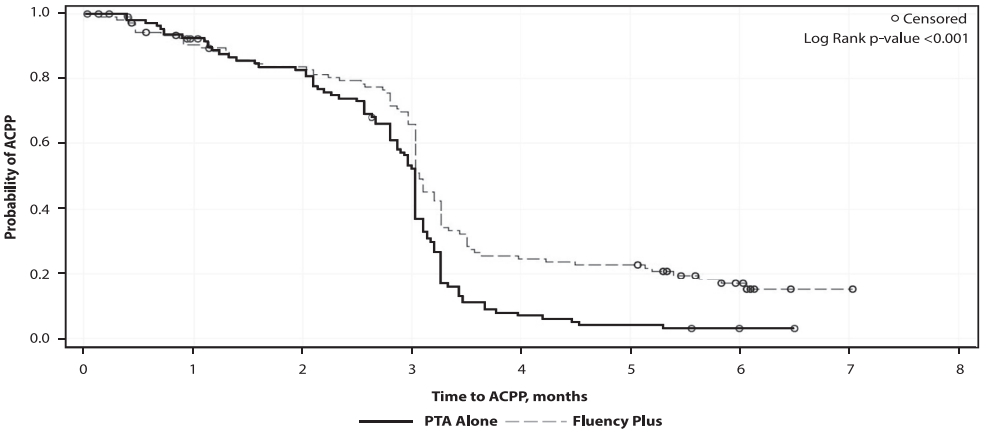
Table 10: Access Circuit Primary Patency at Six Months (ITT)

	PTA Alone (N=111)	Fluency® Plus (N=109)
Percentage of ACPP at 6 months (%)	**3.0**	**16.7**
95% CI for Rate [1]	(0.00, 6.27)	(9.24, 24.16)
Time to event (days)		
Median	91.0	92.0
95% CI for Median [2]	(86.00, 91.00)	(91.00, 98.00)
25% and 75%-ile	70.0, 98.0	84.0, 119.0
Min, Max	1, 195	3, 211
Hazard Ratio (Fluency® Plus over PTA) [3]	0.59	
95% CI	(0.44, 0.79)	
p-value: Fluency® Plus vs. PTA group [4]	<0.001	

[1] The 95% confidence interval uses a normal approximation with Greenwood's estimate of variance.
[2] The 95% confidence interval about median uses the Brookmeyer and Crowley method.
[3] Proportional hazards regression model with treatment term, stratified by AV access type (graft or fistula).
[4] The p-value (one-sided) is based on a stratified log-rank test with strata of AV graft and AV fistula.

Figure 10 presents the Kaplan-Meier curves for Access Circuit Primary Patency through 6 months in the ITT group. The analysis shows a difference in survivorship curves between the treatment groups, with a steeper decline in survivorship for PTA than for **Fluency® Plus Endovascular Stent Graft**, particularly after approximately 3 months.

Figure 10: Kaplan-Meier Analysis for Access Circuit Primary Patency through 6 Month Follow Up (ITT)



SECONDARY EFFECTIVENESS RESULTS

Hypothesis Tested Secondary Effectiveness Result

Post-Intervention Lesion Patency (PLP) at six months was the only secondary effectiveness endpoint used to statistically compare the performance of the **Fluency® Plus Endovascular Stent Graft** to the PTA Control.

Per the protocol, PLP was defined as the interval after the index procedure until the next reintervention at the original treatment site, or until the extremity (access) is abandoned for permanent access.

The PLP was significantly higher ($p<0.001$) in the **Fluency® Plus Endovascular Stent Graft** group (65.2%) than in the PTA Control (10.4%), as detailed in Table 11. The PLP endpoint hazard ratio is 0.18, which translates to an 82% reduction in the risk of failure of PLP due to the use of

Fluency® Plus Endovascular Stent Graft compared to PTA alone.

This demonstrated superiority of the **Fluency® Plus Endovascular Stent Graft** to the PTA Control with respect to Post-Intervention Lesion Patency.

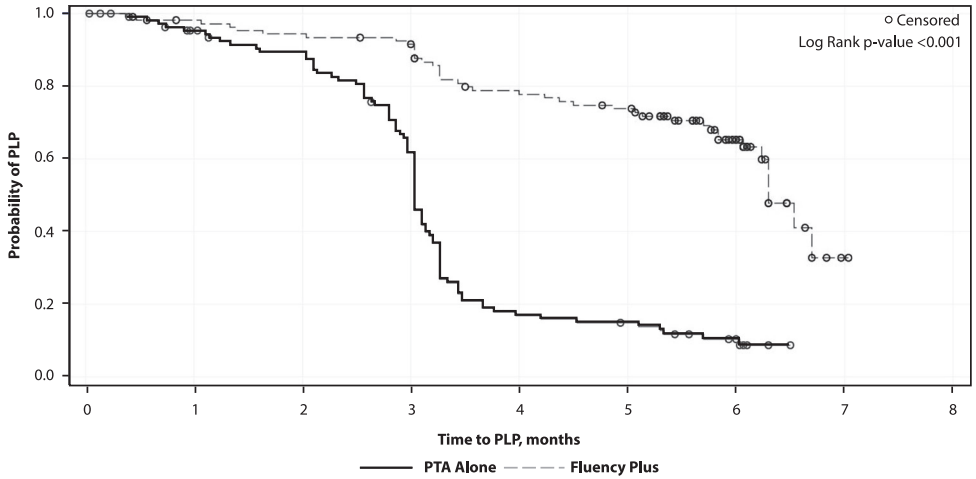
Table 11: Post Intervention Lesion Patency at 6 Months (ITT)

Overall (AV Graft and AV Fistula)		
	PTA Alone (N=111)	**Fluency® Plus (N=109)**
Percentage of Post-Intervention Lesions Patency at 6 months (180 days)	10.4	65.2
95% CI for Rate [1]	(4.30, 16.57)	(55.59, 74.86)
Time to event (days)		
Median	91.0	189.0
95% CI for Median [2]	(91.00, 94.00)	(187.00, NE)
25% and 75%-ile	80.0, 103.0	135.0, NE
Min, Max	1, 195	12, 211

[1] The 95% confidence interval uses a normal approximation with Greenwood's estimate of variance.
[2] The 95% confidence interval about median uses the Brookmeyer and Crowley method. NE = Not estimable.

The Kaplan-Meier analysis for PLP through 6 months (ITT population) is shown in Figure 11. The analysis shows a difference in survivorship curves between the treatment groups, with a noticeably steeper decline in survivorship from 2 months on for the PTA group.

Figure 11: Kaplan-Meier Analysis for Post Intervention Lesion Patency at 6 months (ITT)



Non Hypothesis Tested Secondary Effectiveness Results

The results for the non-hypothesis tested secondary endpoints are listed in Tables 12 and 13.

Table 12: Secondary Effectiveness Results without hypothesis testing (ITT)

	PTA alone (N=111)	Fluency® Plus (N=109)
Index of Patency Function [1]	n=100	n=88
30 Days – mean number of days (SD) 90 Days – mean number of days (SD) 6 Months – mean number of days (SD)	29.5 (3.25) 84.4 (17.61) 125.7 (53.79)	30.0 (0.00) 86.4 (13.60) 137.9 (49.64)
Index of Patency Function at Target Lesion [2]	n=100	n=88
30 Days – mean number of days (SD) 90 Days – mean number of days (SD) 6 Months – mean number of days (SD)	29.5 (3.25) 84.8 (17.16) 136.1 (51.67)	30.0 (0.00) 87.6 (11.34) 153.8 (42.60)
Post-Intervention Secondary Patency [3] 30 Days – Rate (no. events/no. at risk) 90 Days – Rate (no. events/no. at risk) 6 Months – Rate (no. events/no. at risk)	 100.0 (0/103) 100.0 (0/100) 100.0 (0/54)	 100.0 (0/105) 100.0 (0/102) 98.8 (1/55)
Binary Restenosis at 90 Days [4]	74.8% (83/111)	19.3% (21/109)

[1] Index of Patency Function (IPF) was defined as the time from the index study procedure to complete AV graft or AV fistula abandonment divided by the number of visits for a reintervention performed on the AV access circuit in order to maintain vascular access for hemodialysis

[2] Index of Patency Function at Target Lesion (IPF-T) was defined as the time from the index study procedure to complete access abandonment divided by the number of visits for a reintervention performed at the target lesion in order to maintain vascular access for hemodialysis

[3] Post-Intervention Secondary Patency (PSP) was defined as the interval after the index intervention until the access undergoes surgical thrombectomy or revision, or until the access is abandoned.

[4] Lesions with a ≥50% diameter stenosis at 90 days follow-up were characterized as restenotic. If a study patient returned for a reintervention prior to the 90 day (+/- 15 days) Follow-Up Visit, angiographic images were submitted to the Core Lab for Qualitative Vessel Analysis (QVC). If this occurred, a repeat 90 day Follow-Up angiogram was not performed.

Table 13: Acute Secondary Effectiveness Results without hypothesis testing (Randomized Patients)

	PTA alone (N=137)	FLUENCY® PLUS (N=128)
Technical Success (Device Delivery Success) [1]	N/A	99.2% (127/128)
Procedure Success [2]	95.6% (131/137)	96.9% (124/128)

[1] Technical success was defined as deployment of the implant to the intended location assessed at the time of the index procedure.
[2] Procedure Success was defined as anatomic success and resolution of the pre-procedural clinical indicator(s) of a hemodynamically significant stenosis.

Patient Death Summary
There were sixteen (16) deaths among the randomized patients, including 8 patients in the test group and 8 patients in the control group. None of these deaths were attributed to the study device.

The eight (8) deaths in the study device group occurred between 13 days and 158 days following the index procedure. Causes of death included: hemorrhagic shock with multi-organ failure (day 97), myocardial infarction (day 158), septic shock and pneumonia (day 16), one unknown cause of death (day 13), end stage renal disease (day 134), cardiac arrest (day 133), metastatic pancreatic carcinoma (day 129), and sepsis secondary to cellulitis (day 17).

The eight (8) deaths in the PTA Control group occurred between 01 and 145 days following the index procedure. Causes of death included: ventricular fibrillation (day 1), access rupture, exsanguination (day 145), five events of cardiac arrest (one at day 7, one at day 33, one at day 64, one at day 79, and one at day 12), end stage renal disease (day 120).

Observed Device Malfunctions
There were zero (0) device malfunctions reported

CONCLUSIONS DRAWN FROM THE STUDY

Results of the prospective, multi-center, randomized, concurrently-controlled clinical trial demonstrated that the **Fluency® Plus Endovascular Stent Graft** was superior to the PTA Control with respect to six-month Access Circuit Primary Patency and was non-inferior to the PTA Control with respect to safety.

Data from the clinical trial provides a reasonable assurance that the **Fluency® Plus Endovascular Stent Graft** is safe and effective for use in the treatment of in-stent restenosis in the venous outflow of hemodialysis patients dialyzing by either an arteriovenous (AV) fistula or AV graft located in the upper extremities when used in accordance with its labeling.

Labeling issue date: 05/2014

In the event that 3 years have elapsed between this date and product use, the user should contact Bard to see if additional product information is available.

Bard, Advancing the Delivery of Health Care and Fluency are trademarks and/or registered trademarks of C. R. Bard, Inc.
Copyright © 2014 C. R. Bard, Inc. All Rights Reserved.

Symbols used on Labeling

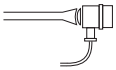
Does Not Contain Natural Rubber Latex

Non-Pyrogenic

Keep Away From Sunlight

Guidewire Compatibility

Keep Dry



Minimum Introducer Size

Single Use

Consult Instructions For Use

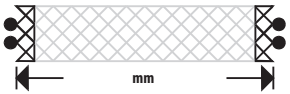
Do Not Resterilize

Do Not Use If Package Is Damaged

MR Conditional

Stent Graft Diameter

Contents: (1)



Stent Graft Length

Manufacturer

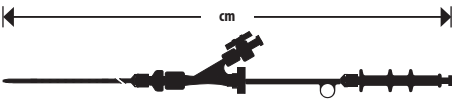
Stent Graft Diameter

Use By

Catalogue Number

Working Length

Lot Number



System Length

Sterilized with Ethylene Oxide

Manufacturer:

Bard Peripheral Vascular, Inc.
1625 West 3rd Street
Tempe, AZ 85281
USA
TEL: 1-480-894-9515
1-800-321-4254
FAX: 1-480-966-7062
1-800-440-5376
www.bardpv.com

BARD | PERIPHERAL VASCULAR

B05667 Rev.4/05-14