TABLE OF CONTENTS

Device Description 2
How Supplied 2
Storage & Handling 2
Indications for Use 3
Compatible Embolic Protection Systems 3
Contraindications 3
Warnings 3
Precautions 4
Potential Adverse Events 4
MR Environment 5
STENT SIZE DETERMINATION 5
Directions for use 5
A PRE-PROCEDURE 5
B INSPECTIONS PRIOR TO USE 6
C DELIVERY SYSTEM PREPARATION 6
D LESION PREPARATION 7
E PROCEDURE 7
F STENT DEPLOYMENT 7
G POST-STENT DEPLOYMENT 9
H PATIENT INFORMATION 10
I INFORMATION ON THE MATERIALS TO WHICH PATIENTS CAN BE EXPOSED 10
J WARRANTY/LIABILITY 10
K REPORTING OF ADVERSE EVENT AND SERIOUS INCIDENT 10
Summary of Primary Clinical Study 11
A Study Design 11
i. Clinical Study Inclusion and Exclusion 11
ii. Follow-up Schedule 12
iii. Clinical Endpoints 14
Primary Endpoint 14
Secondary Endpoints included the following: 14
B Subject Accountability 14
C Study Population Demographics and Baseline Parameters 15
i. Study demographics 15
ii. Subject Medical History 16
iii. Lesion Characteristics 17
iv. Procedure Characteristics 17
D Safety and Effectiveness Results 18
i. Primary Safety and Effectiveness Results 18
ii. Secondary Endpoints Results 19
iii. Adverse Events 23
Symbol Definitions 26

Carefully read all instructions prior to use. Observe all warnings and precautions noted throughout these instructions. Failure to do so may result in complications.

DEVICE DESCRIPTION

The InspireMD CGuard™ Prime Carotid Stent System, also referred to as CGuard Prime, is designed to deliver a self-expanding stent to the carotid arteries using a rapid exchange (Rx) delivery system. The self-expanding stent is constructed of a nickel-titanium alloy (Nitinol) and is covered by a permanent protective micromesh (MicroNet™). The stent is loaded into the Rx delivery system. The delivery system is placed at the intended lesion site, and then the stent is expanded by retraction of a protective sheath. The stent and micromesh remain as a permanent vessel scaffolding implant. Upon deployment, the stent imparts an outward radial force on the arterial wall to establish lumen patency. The stents are available in the size matrix shown in **Table 1.**

TABLE 1: CGUARD PRIME CAROTID STENT SIZE MATRIX

Reference Vessel Diameter (mm)	Length (mm)		
	Diameter (mm)	30	40
6.4 – 7.3	8.0	CND0830	CND0840
7.2 – 8.1	9.0	CND0930	CND0940
8.0 – 9.0	10.0	CND1030	CND1040

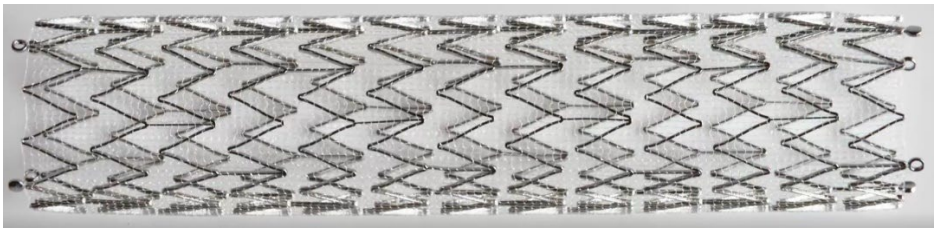


FIGURE 1: CGUARD PRIME CAROTID STENT

The Rx CGuard Prime delivery system is designed with a two-deployment step mechanism: pre-release mechanism (step 1), and stent deployment (step 2), to improve the system operation and allow easy and accurate deployment. This delivery system is suitable for all sizes of CGuard Prime stents. It is comprised of an outer shaft and an inner assembly. A pictorial representation of the delivery system is presented in **Figure 2**.

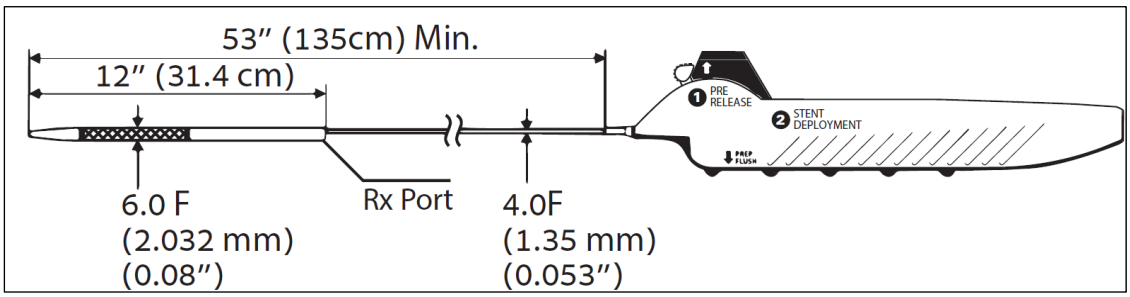


FIGURE 2: RX DELIVERY SYSTEM OF CM WORKING LENGTH

The following accessories are compatible with the CGuard Prime delivery system:

1. 0.014” (0.36 mm) guide wire
2. Emboshield NAV6™ Embolic Protection System (0.014" (0.36 mm) distal protection device)
3. 8F (Inner Diameter >2.20 mm) guiding catheter
4. Vascular sheath 6F (Inner Diameter >2.20 mm)
5. Mo.Ma™ Ultra Proximal Cerebral Protective Device (9F, Inner Diameter >2.12 mm)

HOW SUPPLIED

- The device is supplied sterile, non-pyrogenic and is sterilized by ethylene oxide gas.
- Do not use after the “Use By” (expiration date printed on the label).
- The CGuard Prime is designed for single use only; do not reuse the device.
  Reuse may cause device failure or procedural complications, including device damage, compromised biocompatibility, and contamination, leading to patient harm.

STORAGE & HANDLING

- Store in dry, dark place.
- Handle and dispose of the device and packaging in accordance with acceptable medical practice and applicable local, state, and federal laws and regulations.

INDICATIONS FOR USE

The CGuard Prime Carotid Stent System, when used in conjunction with embolic protection devices specified in the labeling, is indicated for improving carotid luminal diameter in patients at high risk for adverse events from carotid endarterectomy who require carotid revascularization and meet both criteria outlined below:

- Patients with neurological symptoms and ≥ 50% stenosis of the common or internal carotid artery by angiogram, or patients without neurological symptoms and ≥ 80% stenosis of the common or internal carotid artery by angiogram.
- Patients having a vessel with reference diameters between 6.4mm and 9.0mm at the target lesion.

COMPATIBLE EMBOLIC PROTECTION SYSTEMS

The CGuard Prime Carotid Stent System should be used in conjunction with the Abbott Emboshield NAV6™ Embolic Protection System or the Medtronic Mo.Ma™ Ultra Proximal Cerebral Protection Device.

CONTRAINDICATIONS

The CGuard Prime is contraindicated for use in:

- Patients in whom anticoagulant and/or antiplatelet therapy is contraindicated
- Patients with severe vascular tortuosity or anatomy that would preclude the safe introduction, positioning, support, or proper performance of a guide catheter, sheath, or stent system to allow the effective implant
- Patients with known hypersensitivity to nickel-titanium
- Patients with uncorrected bleeding disorders
- Lesions in the ostium of the common carotid artery

WARNINGS

- Only physicians familiar with the principles, clinical applications, complications, side effects, and hazards commonly associated with carotid stent placement should use this device. Preparation of patients receiving the CGuard Prime stent should include initiation of an appropriate dosage of oral antiplatelet medication prior to and following the procedure. Effective anticoagulation therapy should be maintained throughout the procedure and continued into the postoperative period as deemed appropriate by the treating physician.
- Manufacturer's instructions for use should be consulted for all interventional devices used in conjunction with the CGuard Prime stent for their use, contraindications, warnings and precautions.
- Placement of a stent across a bifurcation may preclude future diagnostic or therapeutic procedures.
- As with any type of vascular implant, infection secondary to contamination of the stent may lead to thrombosis, pseudoaneurysm, or rupture.
- The safety and efficacy of the CGuard Prime stent has not been demonstrated with embolic protection systems other than the Emboshield NAV6 and the Mo.Ma Ultra Proximal Cerebral Protection Device.
- The safety and effectiveness of concurrent treatment of lesions in patients with bilateral carotid artery disease have not been established.
- The CGuard Prime stent has not been evaluated for overlapping stent placement. Ensure that the selected stent is sufficiently long for total lesion coverage.
- Do not use contrast material while performing flush preparation to the CGuard Prime delivery system.
- Perform all device exchanges slowly in order to prevent air from being introduced to the system or trauma to the artery.
- Pre-dilating the lesion without embolic protection may increase the risk of an adverse outcome. Implanting a stent or post-dilatation may lead to distal and / or proximal dissection and may cause acute vessel closure, requiring additional intervention (carotid endarterectomy, further dilatation, or placement of additional stents).
- The stent systems may cause thrombus migration from the implant site along the arterial lumen and may produce distal embolization.
- In the event of thrombosis of the expanded stent, thrombectomy or thrombolysis should be considered, and surgical removal of the stent may be required.
- In the event of complications such as infection, pseudo-aneurysm, or fistulation, surgical stent removal may be required.
- Maintain adequate distance between the CGuard Prime System and the distal protection filter to avoid potential engagement or entanglement. If filter engagement and/or filter detachment occurs, additional catheter-based intervention or surgical conversion may be required.
- The delivery system is not designed for use with power injection. The use of power injection may adversely affect device performance.
- Before contrast injection, aspirate any air in the guiding catheter.
- Flush the guiding catheter with saline every time after injecting contrast media.
- Ensure optimal positioning of the stent prior to deployment. Position correction might be performed after the pre-deployment step. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods such as snares and/or forceps may result in additional trauma to the carotid vessel or the vascular access site. Complications may result in vessel dissection, bleeding, hematoma, pseudoaneurysm, stroke, or death.
- Continuously observe the CGuard Prime stent under fluoroscopy during stent deployment.
- DO NOT use the device if the seal or package is torn or broken.
- DO NOT use the product if the EO sterilization indicator on the inner pouch is yellow-brown.
- DO NOT re-use. DO NOT re-sterilize, as this can compromise device performance and may increase the risk of cross-contamination due to inappropriate reprocessing.

PRECAUTIONS

CAUTION: Venous access should be available during carotid stenting to manage possible bradycardia and/or hypotension by either pharmaceutical intervention or placement of a temporary pacemaker if needed.

- Embolic protection of the target vessel is mandatory for all CGuard Prime stent procedures using a compatible distal or proximal embolic protection device (EPD): Emboshield NAV6 Embolic Protection System or the Medtronic Mo.Ma Ultra Proximal Cerebral Protection Device, respectively. The EPD shall be used in accordance with the applicable EPD Instructions for Use.
- Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent.
- The stent and the delivery system are designed to perform as an integrated system and to be used only as designed.
- Do not expose the delivery system to organic solvents, as structural integrity and/ or device function may be impaired.

POTENTIAL ADVERSE EVENTS

Based on the literature and clinical and commercial experience with carotid stents and embolic protection systems, the following list includes possible adverse events associated with these devices:

- Abrupt vessel closure
- Allergic reaction (contrast medium; drug; stent or filter material)
- Amaurosis fugax
- Aneurysm or pseudoaneurysm in the vessel or at the vascular access site
- Angina/coronary ischemia
- Arrhythmia (including premature beats, bradycardia, atrial and/or ventricular tachycardia, atrial and/or ventricular fibrillation)
- Asystole or bradycardia
- Arteriovenous fistula
- Bleeding complications from anticoagulant or antiplatelet medication
- Cardiac tamponade
- Cardiogenic shock
- Carotid artery spasm
- Cerebral edema
- Cerebral haemorrhage
- Cerebral ischemia
- Congestive heart failure (CHF)
- Death
- Detachment and/or implantation of a component of the system
- Dissection of blood vessel
- Distal embolic protection device thrombosis and or occlusion
- Emboli (air, tissue, plaque, thrombotic material, stent)
- Emergency artery bypass graft surgery
- Emergent or urgent carotid endarterectomy
- Emergent surgery to remove stent or distal embolic protection device
- Fever
- Hematoma at the vascular access site, with or without surgical repair
- Hemorrhagic event, with or without transfusion
- Hyperperfusion syndrome
- Hypotension/hypertension
- Infection, local or systemic, including bacteremia or septicemia
- Ischemia/ infarction of tissue organ
- Myocardial infarction
- New or worse encephalopathy
- Pain
- Pain at the catheter insertion site
- Pericardial effusion
- Pulmonary edema
- Renal failure/insufficiency
- Respiratory failure
- Restenosis of the stented segment
- Seizure
- Severe unilateral headache
- Stent/ embolic protection device entanglement/ damage
- Stent/embolic protection device collapse or fracture
- Stent malposition/migration
- Stent thrombosis or occlusion
- Stroke / Cerebrovascular accident (CVA)
- Transient ischemic attack (TIA)
- Tissue necrosis
- Total occlusion of the carotid artery
- Vascular thrombosis/occlusion at the access site, treatment site, or remote site
- Vessel dissection, perforation or rupture

- Vessel spasm or recoil

MR ENVIRONMENT

MRI Safety Information MR Conditional	
A patient with CGuard Prime Carotid Stent may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.	
Parameter	*Condition of Use/Information*
Static Magnetic Field Strength (B_o)	1.5T or 3.0T
Maximum Spatial Field Gradient	20 T/m (2,000 gauss/cm)
RF Excitation	Circularly Polarized (CP)
RF Transmit Coil Type	There are no Transmit Coil restrictions
Operating Mode	Normal Operating Mode
Maximum Whole-Body SAR	2 W/kg (Normal Operating Mode)
Maximum Head SAR	3.2 W/kg (Normal Operating Mode)
Scan Duration and Wait Time	Scan for 60 minutes of continuous RF exposure with one or more MR imaging pulse sequences (scans or series)
MR Image Artifact	The presence of the CGuard Prime Carotid Stent may produce an image artifact that can extend approximately 15 mm from the implant.

STENT SIZE DETERMINATION

The stent sizing is important for successful stenting. Depending on the stent size, a stent shall provide a minimum of 0.5mm -1mm over-size between the stent and vessel. This is recommended in order to achieve optimum sizing and stent expansion of the self-expanding stent (see **Table 2** for reference).

- The stent will expand to accommodate the varying sizes of the internal carotid artery, bifurcation, and common carotid artery. Thus, the stent sizing should be determined usually by the common carotid artery diameter. For example, select a 8.0 mm stent to treat a 6.4 – 7.3 mm diameter vessel. Select a 9.0 mm stent to treat a 7.2 – 8.1 mm diameter vessel.
- The mean percentage of foreshortening for all stent sizes is less than 10% (see **Table 2**). The optimal length size is the shortest stent length consistent with total lesion coverage plus the safety margins.

WARNING

- The CGuard Prime stent is contraindicated for use with lesions in the ostium of the common carotid and aorta.
- Appropriate sizing of the stent to the vessel is required to reduce the possibility of stent migration.
- The CGuard Prime stent has not been evaluated for overlapping stent placement. Ensure that the selected stent is sufficiently long for total lesion coverage.

TABLE 2: STENT FORESHORTENING DATA

Reference Vessel diameter [mm]	**Stent Labeled diameter [mm]**	**Average Foreshortening [%]**	**Unconstrained stent diameter [mm] (After deployment)**
6.4 -7.3	8	2.6	>7.6
7.2- 8.1	9	1.9	>8.4
8.0-9.0	10	2.3	>9.3

DIRECTIONS FOR USE

A **PRE-PROCEDURE**

Patient preparation and sterile precautions should be the same as for any angioplasty procedure. The placement of the carotid stent in a stenotic or obstructed carotid artery must be done in a procedure room with angiography capabilities. Angiography should be performed to map out the extent of the lesion and the collateral flow. Access vessels must be sufficiently patent to proceed with further intervention.

CAUTION: Do not use if the package is damaged, unintentionally opened, or exposed to environmental conditions outside of those specified on the label before use.

B INSPECTIONS PRIOR TO USE

- Inspect the CGuard Prime protective packaging (pouch). Ensure that the pouch is sealed and in an undamaged/non-deformed state.
  CAUTION: Do not use the system if the protective packaging is found to be damaged.
- The operating assistant (non-sterile assistant) should open the protective packaging, and the sterile operator should take the system tray out of the protective packaging (pouch).
- All the following steps described below should be performed by the physician (a sterile operator);
- Carefully remove the CGuard Prime System from the hoop and out of its tray. Lay the device flat. Take care not to kink the shaft of the Rx delivery catheter system.
- Inspect the delivery system handle for any damage (see **Figure 2**).
- Inspect the Rx delivery system distal shaft and tip to verify that it has not been damaged during shipment.
- Ensure that the stent is fully covered by the delivery system shaft.

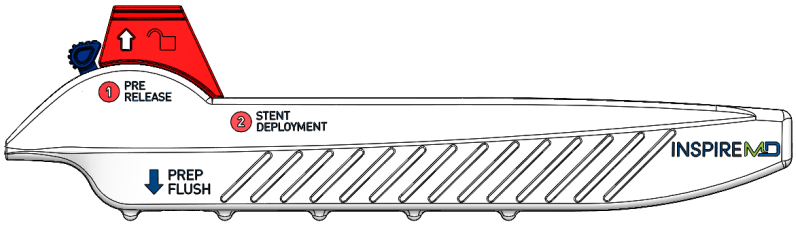


FIGURE 2: DELIVERY SYSTEM HANDLE

CAUTION: The Rx delivery system has an internal shaft. Take care to avoid unnecessary handling, which may kink or damage the delivery system. Keep the Rx delivery system as straight as possible and the delivery handle stationary during deployment. Do not use the device if it is kinked.

CAUTION: Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is especially important during delivery system removal from packaging, placement over the distal embolic protection device wire, and advancement through a hemostatic valve and guiding catheter hub.

CAUTION: The stent on the Rx delivery system is intended to perform as a system. Do not remove the stent from the delivery system, as removal may damage the stent. If removed, the stent cannot be placed back on the Rx delivery system.

C DELIVERY SYSTEM PREPARATION

- For device flushing, connect a 3 mL or 5 mL luer lock syringe to the “PREP FLUSH” port (see figure 4) filled with heparinized saline solution (DO NOT USE CONTRAST), maintain positive pressure until saline fluid drops are observed exiting the CGuard Prime at the distal end. This process may take up to 30 seconds. Ensure saline is observed at the distal end as well as at the Rx guide wire port.
- At the end of the flushing process, remove the syringe.
- The system is flushed.
- Keep the device straight and flat to avoid kinking the shaft.
- Special care must be taken not to handle or in any way disrupt the stent on the delivery system. This is most important during catheter removal from packaging, placement over the guidewire, and advancement through the hemostasis valve and guiding catheter or vascular sheath.
- Do not attempt to deploy the stent from its delivery system while the system is not located in the target lesion. If deployed, the stent cannot be retrieved back into the delivery system, and the stent may become damaged.

CAUTION: Make sure to flush the system with at least 2 mL of saline.
CAUTION: Ensure correct flushing is performed in order to remove all air from the delivery system and eliminate the chance of friction within the sheath.
CAUTION: Ensure that CGuard Prime is fully flushed with heparinized saline prior to use. Do not use the CGuard Prime if flushing is not visible exiting at the distal end of the catheter.
CAUTION: Do not use contrast material while flushing.

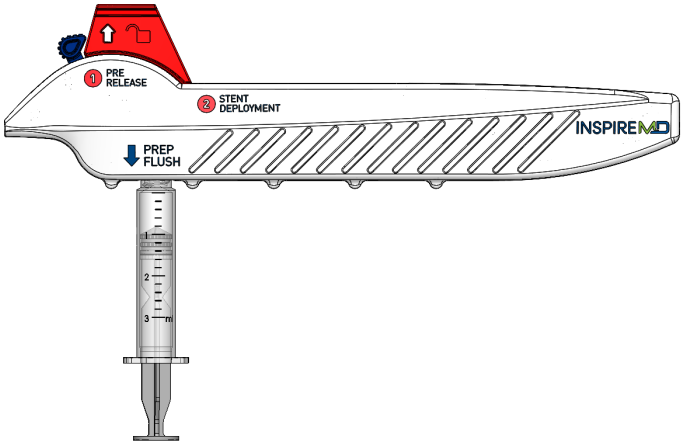


FIGURE 3: EXAMPLE OF 3 ML LUER LOCK SYRINGE CONNECTED TO THE CGUARD PRIME FOR FLUSHING

D LESION PREPARATION

- Maintain the patient's Activated Clotting Time (ACT) at > 250 seconds throughout system usage.

  WARNING: Administer a heparin dose sufficient to maintain an ACT of > 250 seconds to prevent thrombus formation on the devices.
  CAUTION: Venous access should be available during carotid stenting to manage bradycardia and/or hypotension by a pacemaker placement or pharmaceutical intervention if needed.
  CAUTION: The CGuard™ Prime must be used with a guiding catheter or vascular sheath to maintain adequate support of the 0.014" (0.36 mm) guidewire throughout the procedure.
  CAUTION: The system is not compatible with guidewires larger than 0.014" wire (0.36 mm).
  CAUTION: Use of automatic bleed back control hemostatic valves is not recommended.
  CAUTION: When the catheter is in the body, it should be manipulated only under fluoroscopy. Radiographic equipment that provides high-quality images is needed.
  WARNING: Perform all catheter exchanges slowly in order to prevent air embolism or trauma to the artery.

- It is mandatory to use a Mo.Ma Ultra Proximal Cerebral Protection Device or Emboshield NAV6 distal embolic protection device with the CGuard Prime System. The CGuard Prime System has not been tested before compatibility with other embolic protection devices.
- If required, pre-dilate the lesion with an appropriate-size balloon dilatation catheter to a minimum of 3.0 mm after the distal protection device is in place beyond the lesion.
  Note: If no pre-dilatation balloon is utilized, there must be a minimum luminal opening of 3.0 mm to enable retrieval of the tip of the CGuard Prime delivery system.
- Maintain the embolic protection device stationary while withdrawing the balloon catheter.

E PROCEDURE

- If lesion pre-dilatation has been performed, remove the balloon catheter and load the delivery system onto the 0.014" (0.36 mm) guide wire.

  CAUTION: The delivery system is not designed for use with a power injector. Use of a power injector may adversely affect device performance.

- Keep the device flat to avoid kinking the shaft.
- Insert the Rx delivery system through the hemostatic valve adapter. Ensure that the hemostatic valve of the guiding sheath/ guiding catheter is open to allow freedom of movement of the delivery system outer sheath during deployment.

  CAUTION: If resistance is encountered during the Rx delivery system introduction, the system should be withdrawn and a new system used.

- Advance the stent and the Rx delivery system forward under fluoroscopic guidance to the lesion site.

  CAUTION: Avoid any tension in the Rx delivery system prior to deployment.

F STENT DEPLOYMENT

- The deployment mechanism contains two steps:
  Step 1 – Pre-deployment – in this step, the stent is advanced toward the distal end of the catheter sheath
  Step 2 – Deployment – in this step, the catheter is retracted, and the stent is deployed.

  CAUTION: Ensure that the hemostatic valve of the guiding sheath/guiding catheter is open before the pre-deployment step and during deployment to allow the delivery system outer sheath-free movement.

- Catheter positioning at target lesion:
- Ensure optimal positioning of the stent prior to deployment. Once deployment is initiated, the stent cannot be repositioned or recaptured. Stent retrieval methods (use of additional wires, snares, and/or forceps) may result in additional trauma to the carotid vasculature and/or vascular access site. Complications may include death, stroke, bleeding, hematoma, or pseudoaneurysm.

- Confirm the stent position angiographically prior to deployment. Adjust position, if necessary, after the pre-deployment step.

Step 1 – Stent Pre-deployment

- When the target location is achieved, squeeze the safety tab with your fingers to release the tab and remove the safety tab. Discard the tab. See Figure 4 and **Figure 5** below for a visual demonstration of the start and end positions of the safety tab removal step.

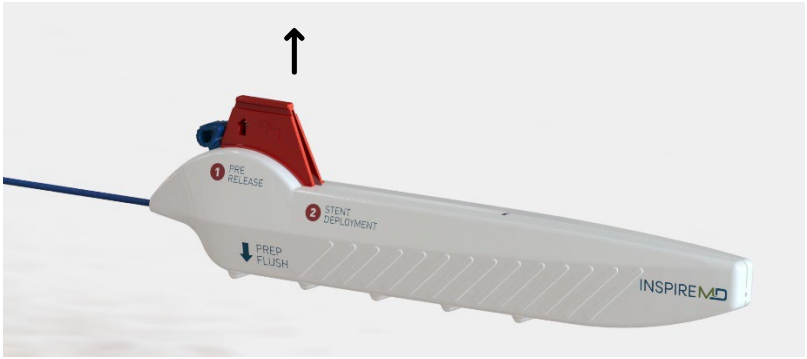


FIGURE 4: SAFETY TAB REMOVAL START POSITION

FIGURE 5: SAFETY TAB REMOVAL END POSITION

Note: Ensure that the Rx delivery system is straight and not coiled. Keep the Rx delivery system stationary during deployment. Do not restrain the main shaft of the Rx delivery catheter during deployment. It must be free to move.

- The system is ready for stent deployment.

- Carefully retract the lever along the top arc. This is the pre-deployment step. See **Figure 6** below for a visual demonstration of the pre-deployment step.

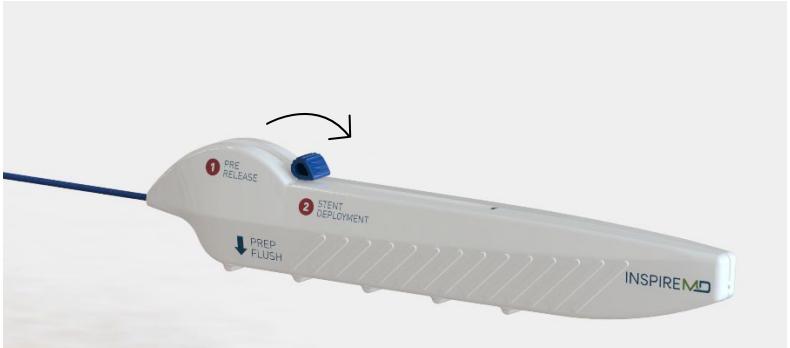


FIGURE 6: PRE-DEPLOY END POSITION

- Following pre-deployment, check stent positioning and if required, immediately perform a location adjustment. The system lever is now locked in place and ready for Step 2- stent deployment.

  CAUTION: The stent location cannot be adjusted once Step 2- stent deployment has begun.

Step 2 – Stent Deployment

- Carefully retract the lever along the top plane of the handle until the lever reaches the end of its stroke. This is the stent deployment step. See **Figure 7** and **Figure 8** below for a visual demonstration of the start and end positions of the stent deployment step.

  Note: Before the beginning of the deployment step, ensure that the previous step, pre-deployment, was completed. i.e., the blue lever is located on the lowest point of the arc, ready to be pulled back along the straight plane.

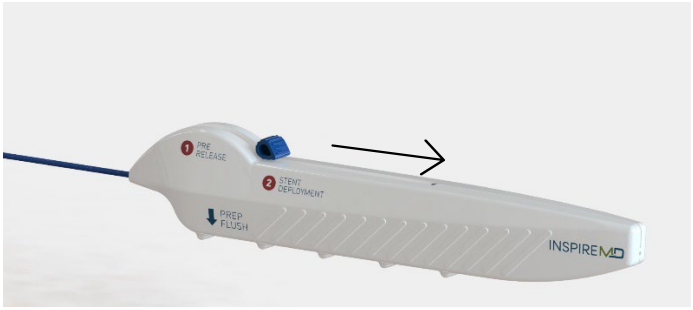


FIGURE 7: STENT DEPLOY START POSITION

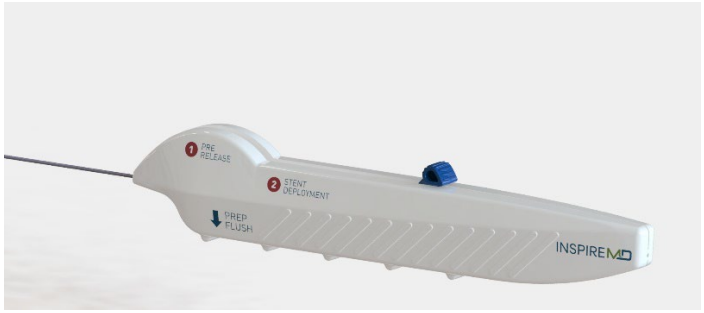


FIGURE 8: STENT DEPLOY END POSITION

  Note: If significant resistance is encountered during lever retraction for deployment and before stent release is initiated, stop this action and remove the system. Once stent deployment is initiated, the stent cannot be recovered back to the sheath.

  CAUTION: Once stent placement has been initiated, do not attempt to pull a partially expanded stent back through the guiding catheter or vascular sheath, as dislodgement of the stent from the Rx delivery system may occur.

  CAUTION: In the event of partial deployment of the stent as the result of the inability to fully deploy the stent, remove the entire Rx delivery system from the patient by pulling it gently backward. This may result in damage to the vessel wall and may require surgical intervention.

  CAUTION: Do not return the deployment lever back to its home position once the deployment step has begun or completed.

- Under fluoroscopy, confirm that the stent has been deployed at the target lesion.

G POST-STENT DEPLOYMENT

- After stent deployment, carefully withdraw the white distal tip of the Rx delivery system through the stent. Then, carefully withdraw the delivery system out of the patient body.

  CAUTION: Ensure that the Rx delivery system is entirely removed from the patient. Once the Rx delivery system is out of the patient, you should be able to remove it from the guiding wire entirely.

- If additional stent-to-wall apposition is desired or to facilitate the use of other interventional devices, the stent can be post-dilated with a balloon dilatation catheter. Do not expand the stent beyond its unconstrained maximum diameter, as stated on the label and in **Table 2**. Post-dilate as needed in accordance with the compliance chart accompanying the selected balloon catheter.

  CAUTION: Care must be exercised when crossing a newly deployed stent with other interventional devices to avoid disrupting the stent geometry and placement of the stent.

  WARNING: Overstretching of the artery may result in artery rupture and life-threatening bleeding.

- Following stent placement, an angiogram should be performed to document the stent's final result and vessel patency.

- Upon completion of the angiogram, the embolic protection device should be removed in accordance with the instructions for use with that device.

- Patients should be put on an appropriate regimen of anticoagulants/antiplatelets.

H PATIENT INFORMATION

A patient implant card, which contains identifying information about the implanted device, is included in the device package. After the device is implanted, complete the patient implant card and provide it to the patient before they are discharged.

Healthcare providers should communicate the following instructions to their patients:
- Always carry their implant card with them.
- Always inform any healthcare personnel that they have an implanted device before any procedure.

I INFORMATION ON THE MATERIALS TO WHICH PATIENTS CAN BE EXPOSED

The implant, self- expanding stent is constructed of a nickel titanium alloy (Nitinol) and is covered by a permanent protective micromesh made of polyethylene terephthalate (PET). The delivery system, which the patient is exposed for short time is constructed of Stainless steel, Pebax, Polyimide, Polyethylene terephthalate (PET), Polyolefin & Polytetrefluoroethylene (PTFE).

J WARRANTY/LIABILITY

The product and each component of its system have been designed, manufactured, tested and packaged with all reasonable care. The warnings contained in InspireMD instructions for use are expressly considered as an integral part of this provision. InspireMD warrants the product until the expiration date indicated on it or its packaging. The warranty is valid provided that the use of the product was consistent with the instructions for use. InspireMD disclaims any warranty of merchantability or fitness for a particular purpose of the product. InspireMD is not liable for any direct, indirect, incidental or consequential damages caused by the product. Except in the case of fraud or grave fault on the part of InspireMD, compensation of any damage to the buyer will not, in any event, be greater than the invoice price of the disputed products. The guarantee contained in this provision incorporates and substitutes the legal guarantees for defects and compliance, and excludes any other possible liability of InspireMD, however originating, from its product supplied.

These limitations of liability and warranty are not intended to contravene any mandatory provisions of law applicable. If any clause of the disclaimer is considered by a competent court to be invalid or to be in conflict with the applicable law, the remaining part of it shall not be affected and remain in full force and effect. The invalid clause shall be substituted by a valid clause which best reflects InspireMD legitimate interest in limiting its liability or warranty. No person has any authority to bind InspireMD to any warranty or liability regarding the product.

K REPORTING OF ADVERSE EVENT AND SERIOUS INCIDENT

Contact the Customer Service Center with any feedback via the website https://www.inspiremd.com or email complaints@inspiremd.com & customerservice@inspiremd.com or call 1-786-425-3292.

SUMMARY OF PRIMARY CLINICAL STUDY

A clinical study was performed to establish a reasonable assurance of safety and effectiveness of the CGuard Prime Carotid Stent System in human subjects for the treatment of carotid artery stenosis at elevated risk for adverse events following carotid endarterectomy (CEA).

A Study Design

Patients were treated between July 22, 2021, and June 23, 2023. The database reflected data collected through August 20, 2024, and included 317 patients (316 pivotal and 1 roll-in patients) at 24 investigational sites (19 US and 5 OUS sites).

The study was an international, multicenter, single-arm, prospective study to evaluate the safety and effectiveness of the CGuard/CGuard Prime for the treatment of carotid artery stenosis in subjects with high risk for adverse events from carotid endarterectomy. The CGuard and CGuard Prime carotid stent systems include the same implantable stent and only differ in the design of their delivery systems handles. CGuard Stent System was used in 284 patients and CGuard Prime Stent System in 32 patients. These two iterations will hereafter be referred to as "CGuard Prime."

The primary composite safety and effectiveness endpoint was the incidence of the following Major Adverse Events: Death (all-cause mortality), all Stroke, and Myocardial Infarction (DSMI) through 30-days post-index procedure, or ipsilateral stroke between 31 and 365 days. All primary endpoint events were adjudicated by the study independent Clinical Event Committee (CEC).

The endpoint was compared to a performance goal (PG) based on published carotid stenting studies selected based on criteria which included high risk for carotid endarterectomy patients, clear categorization of rates for symptomatic and asymptomatic patients and studies associated with previously approved devices. The PG was set to 11.6%. The sample size was determined on enrollment of 25% symptomatic patients and 75% asymptomatic patients and 10% non-evaluable patient at 1-year. Based on these assumptions, an evaluable sample size of 316 subjects provided 80% power to reject the null hypothesis with a one-sided type I error rate of 0.025. The null hypothesis was tested on the ITT population at a one-sided 0.025 level of significance using the one-sided Z-test. If the upper bound of the two-sided 95% confidence interval calculated from the observed primary endpoint rate was < 11.6% and the p-value wasless than 0.025, the null hypothesis would be rejected (i.e. performance goal was met).

The study had three patient populations: Intent-to-Treat (ITT), modified-ITT (mITT) and Per Protocol (PP). The ITT analysis population includes all enrolled subjects who gave informed consent, who met all eligibility criteria, were approved by the Screening Committee and in whom the study device entered the vasculature. The mITT population was the subset of the ITT analysis population who were implanted with the CGuard Prime device. The PP population was the subset of the mITT analysis population with no major protocol deviations. Primary endpoint analysis at 1 year is performed on the number of evaluable patients remaining in each population (ITT, mITT, and PP). See **Figure 9** for details.

Secondary endpoints included technical success, treatment success, the incidence of individual MAE, in-stent restenosis (ISR), target lesion revascularization (TLR), as defined below. Secondary endpoints were descriptive only, with no formal hypothesis testing.

The Data Safety Monitoring Board (DSMB) reviewed all study safety data on a regular basis and advised on the continuing safety, validity and scientific merit of the study. All vascular imaging required for the study was evaluated and analyzed by an independent core lab.

i. Clinical Study Inclusion and Exclusion

Enrollment in the C-GUARDIANS study was limited to patients who met the following inclusion criteria.

General Inclusion Criteria:

- Subject is ≥ 19 years and ≤ 80 years of age.
- Subject is willing and able to provide appropriate study-specific informed consent. follow protocol procedures, and comply with follow-up visit requirements.
- Subject is willing and able to take dual antiplatelet therapy for a minimum of 30 days.
- Life expectancy ≥ 24 months from the date of the index procedure.
- Females who are not pregnant or lactating and not planning to become pregnant for the duration of the study.
- Subject has a modified Rankin Score of ≤ 2 at the time of informed consent.
- Subject is either:
    - Symptomatic with carotid stenosis ≥ 50%. Symptomatic is defined as amaurosis fugax, transient ischemia attack (TIA) or stroke within the last 6 months ipsilateral to the side of the stenosis.
    - Asymptomatic with carotid stenosis ≥ 80%.

High-risk Inclusion Criteria:
For inclusion in the study, a subject must have qualified in at least one high-risk condition, as shown below.

Co-morbid Conditions:

- Age ≥ 70.
- CCS angina class 3-4 or unstable angina.
- Congestive Heart Failure (CHF) NYHA class III-IV.
- Left ventricular ejection fraction (LVEF) ≤ 35%.

- MI ≥ 72 hours and < 6 weeks pre-procedure.
- Multi-vessel CAD (≥ 2 vessels >70% stenosis) and history of angina.
- Chronic Obstructive Pulmonary Disease (COPD) with FEV1<50.
- Permanent contralateral cranial nerve injury/paralysis.
- Restenosis from previous carotid endarterectomy (CEA).
- Planned coronary artery bypass grafting (CABG) or valve replacement surgery between 31-60 days after CAS.
- Abdominal Aortic aneurysm surgical repair or Endovascular repair is planned between 31 to 60 days after CAS.

Anatomic Conditions:

- Occlusion of the contralateral CCA or ICA.
- Prior radiation treatment to the neck or a radical neck dissection.
- Severe bilateral ICA stenosis requiring treatment.
- Target lesion at or above the level of the jaw (C2) or below the clavicle.
- Severe tandem lesions.
- Inability to extend the neck due to cervical disorders.
- Laryngeal palsy or laryngectomy.
- Prior head and neck surgery in the region of the carotid artery.
- Tracheostomy or tracheostoma.
- Spinal immobility of the neck.
- Hostile neck or surgically inaccessible lesion.

Angiographic General Inclusion Criteria
For inclusion in the study, a subject must have all the following imaging criteria:

- Target lesion location at the carotid bifurcation and/or proximal internal carotid artery (ICA).
- Vessel distal to target lesion can accommodate embolic protection device (EPD) with either the Emboshield NAV6 distal protection device OR the Mo.Ma proximal embolic protection device
- Diameter at stent landing zone is 4.8 mm to 9.0 mm.
- Target lesion length ≤ 36 mm, that can be covered by a single CGuard Prime Stent.

Patients were <u>not</u> permitted to enroll in the C-GUARDIANS study if they met any of the following exclusion criteria:

- Planned interventional procedure or surgery of the carotid, coronary or peripheral arteries within 30 days before or after the index carotid procedure.
- Severe vascular anatomy that would preclude safe sheath insertion, deliverability of stent or embolic protection device.
- Type III aortic arch.
- Total occlusion of the target vessel.
- Presence of “String sign” of the target lesion.
- In-tandem lesions with ≥ 50% or ≥ 80% diameter stenosis for symptomatic or asymptomatic patients, respectively, which cannot be covered by a single CGuard Prime stent.
- History of bleeding diatheses or coagulopathy.
- Bilateral carotid stenosis requiring treatment on both sides within 30 days prior to or following planned index procedure.
- Subject is on renal replacement therapy or has Stage 4 or 5 Chronic Kidney Disease (CKD).
- Known reason for potential stroke other than carotid artery stenosis, including history of atrial fibrillation or other sources of thromboemboli within the past 12 months.
- History of thrombophilia.
- Known sensitivity or allergy to nitinol or titanium.
- Sensitivity to contrast media that cannot be adequately pre-treated.
- Sensitivity to both forms of protocol-acceptable anticoagulation strategies (i.e., both heparin AND Bivalirudin).
- Sensitivity to an antiplatelet agent AND all protocol acceptable alternative antiplatelet options.
- Previous stent placement in the target vessel.
- Evolving stroke or intracranial hemorrhage, or history of previous intracranial hemorrhage or brain surgery within the past 12 months.
- Major neurologic deficit with NIHSS of ≥ 15.
- Dementia or other neurologic condition confounding the neurologic assessment.
- Clinical condition that, in the opinion of the investigator, makes endovascular therapy impossible or hazardous.
- Subject previously enrolled in this clinical trial.
- Possible/probable non-compliance of subject with protocol required follow up or medication.
- Subject is currently participating in another clinical trial that has not completed its primary endpoint assessment or would confound this C-GUARDIANS Pivotal IDE Clinical Study.

ii. <u>Follow-up Schedule</u>

All patients were scheduled to return for follow-up examination at 30 days (-1/+7 days), 6 months (± 30 days), 1 year (± 30 days), and 2 and 3 years (± 60 days) postoperatively, as shown in **Table 3** below. Adverse events and complications were recorded at all visits.

To determine subject eligibility, a screening committee reviewed imaging data, along with patient medical history, for assessment of inclusion criteria, and approval prior to the study procedure.

The screening committee was comprised of an interdisciplinary team of study investigators with pertinent knowledge in carotid stenting. Prior to a subject being enrolled in the study, the investigational site received confirmation from the screening committee that the subject was eligible to be enrolled.

TABLE 3: SCHEDULE OF EVENTS

Test/Assessment	Screening	Baseline	Index Procedure	Discharge or 96 hours post-procedure	30 Day (-0, +7D) (10)	180 Day (± 30D)	1-Year (± 30D)	2- & 3- Year (± 60D)	Unscheduled Visit	Early Withdrawal
Study Visit No.	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8 & 9**	--	--
Study Consent	X									
Medical History	X									
Concomitant Medications	X	X	X	X	X	X	X	X	X (8)	X (9)
Targeted Physical Exam	X (1)			X	X	X	X	X	X (8)	X (9)
NIH Stroke Scale (2)		X		X	X	X	X	X	X (8)	X (9)
Modified Rankin Scale (mRS)	X (1)				X	X	X	X	X (8)	X (9)
Carotid Duplex Ultrasound	X (3)				X	X	X	X	X (8)	X (9)
Cerebral Angiography or Computed Tomography Angiography (CTA) and Magnetic Resonance Angiography (MRA) (MRA)	X (4)		X							
Head Computed Tomography or Brain Magnetic Resonance Imaging	X (5)									
Index procedure			X							
12-lead ECG	X (1)			X					X (8)	
Complete Blood Count	X (1)			X					X (8)	
Coagulation Panel/ International normalized ratio for subjects on Vitamin K antagonists	X (1)			X	X	X	X	X	X (8)	X (9)
Chemistry Panel (BUN, Creatinine)	X (1)									
Cardiac Biomarkers (troponins or CK-MB)		X		X (6)						
Pregnancy Test (7)		X								
Adverse Events	X	X	X	X	X	X	X	X	X	X

(1) May be obtained at either Screening or Baseline visit.

(2) Neurological assessment must be performed by a physician or other study team personnel certified in administration of the National Institute of Health Stroke Scale (NIHSS).

(3) Bilateral carotid duplex ultrasound is required within 180 days of the screening visit. The pre-procedure ultrasound is not sent to the core lab.

(4) Cerebral angiography or CTA showing the Internal Carotid Artery (ICA), Common Carotid Artery (CCA) and aortic arch is required 90 days prior to the procedure.

(5) Head CT or Brain MRI is required for symptomatic patients within 180 days of the screening visit.

(6) Routine collection for all subjects at approximately the following post-index procedure intervals: 12-24 hours, 36-48 hours, 72 hours or at discharge. Thereafter, if cardiac biomarkers remain elevated, collect daily until values show a decline.

(7) Urine or serum pregnancy test is acceptable.

(8) To be performed as clinically indicated.

(9) Test/assessments to be performed to the extent possible.

(10) If the CGuard Prime carotid stent system with EPD enters the vasculature and is unsuccessful, a telephone follow-up visit is required at 30 days (+/-7 days).

iii. Clinical Endpoints

Primary Endpoint

The primary endpoint is the composite of the incidence of the following Major Adverse Events: Death (all-cause mortality), all Stroke, and Myocardial Infarction (DSMI) through 30-days post-index procedure, or ipsilateral stroke between 31- and 365-day follow-up, based on Clinical Events Committee (CEC) adjudication.

Strokes were defined as acute episodes of local or global neurological dysfunction caused by brain, spinal cord, or retinal vascular injury as a result of hemorrhage or infarction. Strokes were further categorized as major (NIHSS is ≥ 6 or based on clinical data at least 30 days after the date of stroke onset) or minor (i.e. a non-major stroke). Strokes occurring between 31 and 365 days were considered ipsilateral strokes if involving the anterior circulation (the internal carotid artery, the middle cerebral artery, the anterior cerebral artery, or more proximal intracranial branch of the internal carotid artery) on the same side as the stented carotid artery.

Myocardial infarctions were defined by two methods: the Fourth Universal Definition of MI (UDMI) and the Academic Research Consortium (ARC)-2 definitions. The primary endpoint was analyzed using each definition independently. The primary analysis was conducted using the ARC-2 definition. A sensitivity analysis confirmed similar results using the UDMI definition.

Secondary Endpoints included the following:

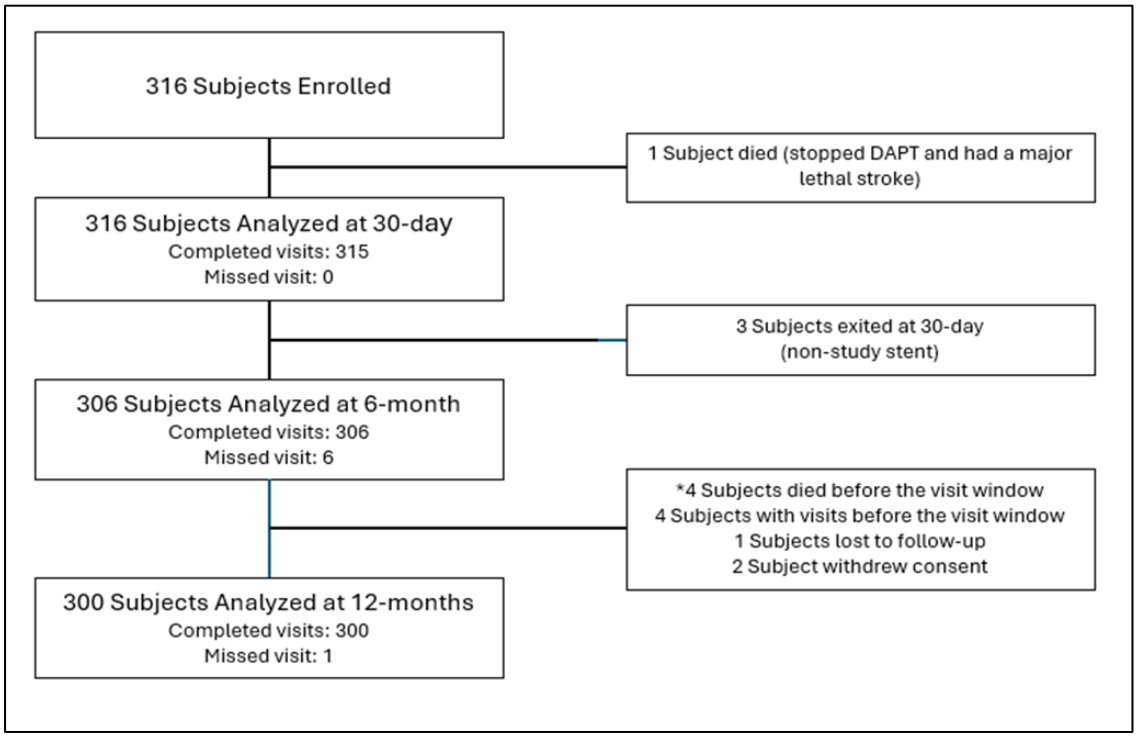
- Incidence of the following composite of Major Adverse Events: Death (all-cause mortality), all Stroke, and Myocardial Infarction (DSMI) through discharge, 30-days, 6-months, and 1-, 2-, 3-year follow-up, based on CEC adjudication.
- Incidence of each individual component of the Major Adverse Events: Death (all-cause mortality), all Stroke, and Myocardial Infarction (DSMI) through discharge, 30-days, 6-months, and 1-, 2-, 3-year follow-up, based on CEC adjudication.
- Ipsilateral stroke through discharge, 30 days, 6 months and 1-, 2-, 3-year follow-up.
- Ipsilateral major stroke through discharge, 30 days, 6 months and 1-,2-,3-year follow-up.
- Incidence of In-stent Restenosis (ISR) > 70%. ISR > 70% is defined as PSV > 300 cm/s associated with stent, or vessel occlusion based on transcervical duplex ultrasound through 1-, 2-, 3-year follow-up. Based on Imaging Core Laboratory assessment. Will be further categorized based upon the presence or absence of symptoms associated with restenosis.
- Incidence of In-stent Restenosis (ISR) > 50%. ISR > 50% is defined as PSV > 220 cm/s associated with stent, or vessel occlusion based on transcervical duplex ultrasound, through 1-, 2-, 3-year follow-up evidenced by Imaging Core Laboratory assessment. Will be further categorized based upon the presence or absence of symptoms associated with restenosis.
- Incidence of Target Lesion Revascularization (TLR) through 1-, 2, 3-year follow-up. TLR is defined as clinically driven revascularization procedure of the original treatment site, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter within the stented lesion or within 5 mm proximal or distal to the index stent.
- Ipsilateral stroke, stent thrombosis, cardiovascular death or other device related clinical events from discharge up to 1-, 2-and 3-year follow-up.
- Primary endpoint for subjects that adhere to antiplatelet pharmacology.
- Technical Success Rate defined as the number of subjects with at least one study stent that is successfully delivered and deployed with final residual diameter stenosis < 30% following final post-balloon dilatation, if performed. Based on quantitative angiography measurements at time of index procedure.
- Treatment Success Rate defined as the number of subjects who meet CGuard Prime Technical Success Rate without experiencing Major Adverse Event (based on CEC adjudication) through 30 Days, divided by the total number of subjects where stent deployment was attempted.

B Subject Accountability

At the time of database lock, of 316 patients enrolled in the study, 94.9% (n=300) were still available for ITT analyses at 12-months.

A summary of subject disposition per ITT analysis is presented in **Figure 9.**

FIGURE 9 - SUBJECT DISPOSITION PER ITT ANALYSIS



*Four (4) subjects died between 31 days and the opening of the 12-month visit window and were therefore not evaluable for analysis at 12-month in the ITT analysis.

The primary analysis of safety and effectiveness was based on the ITT population of 316 subjects with 300 patients with evaluable primary endpoint information through 1 year.

Of the ITT analysis population of 316 subjects, 16 subjects were not included in the primary endpoint proportion. The reasons for these subjects not being included are the following: three (3) study device not implanted and subsequently exited the study at 30 days, one (1) lost to follow-up prior to 1 year follow-up, two (2) withdrew informed consent prior to 1 year follow-up, two (2) 12-month visit not performed and subject not yet exited, four (4) 12-month visit performed prior to window opening and no subsequent visit performed, and four (4) deaths occurred between 31 days and the 12-month visit window opening (day 335).

Of the mITT analysis population of 313 subjects, thirteen (13) subjects were not included in the primary endpoint proportion. The reasons for these subjects not being included are the following: one (1) lost to follow-up prior to 1 year follow-up, two (2) withdrew informed consent prior to 1 year follow-up, two (2) 12-month visit not performed and subject not yet exited, four (4) 12-month visit performed prior to window open and no subsequent visit performed, and four (4) deaths occurred between 31 day and the 12-month visit window opening (day 335).

Of the PP analysis population of 295 subjects, nine (9) subjects were not included in the primary endpoint proportion. The reasons for these subjects not being included are the following: one (1) lost to follow-up prior to 1 year follow-up, one (1) withdrew informed consent prior to 1 year follow-up, three (3) 12-month visit performed prior to window open and no subsequent visit performed, and four (4) death occurred between the 31 day visit window opening (day 335).

C Study Population Demographics and Baseline Parameters

i. Study demographics

The ITT population was predominately men (64%) and Caucasian (97%). Median age was 70 years, Subject demographics are summarized in **Table 4**. The demographics of the study population are typical for a carotid artery study performed in the U.S.

TABLE 4: SUBJECT DEMOGRAPHICS

Subject Demographics	ITT (N = 316)
Sex	
Female	36.1% (114)
Male	63.9% (202)
Age	
Mean ± SD	69.0 ± 6.6

Subject Demographics	ITT (N = 316)
Median	70.0
Min, Max	47, 80
Race	
American Indian or Alaska Native	0.3% (1)
Asian	0.0% (0)
Black or African American	1.9% (6)
Native Hawaiian of Other Pacific Islander	0.3% (1)
Caucasian	97.2% (307)
Other	0.3% (1)
Ethnicity	
Hispanic or Latino	10.1% (32)
Not Hispanic or Latino	88.3% (279)
Unknown	1.6% (5)
Current Alcohol Use	
None	72.5% (229)
≥1 drinks/week	27.5% (87)
Smoking History	
Never Smoked	26.6% (84)
Current Smoker	26.3% (83)
Former Smoker	47.2% (149)

ii. Subject Medical History

A summary of subject medical history is provided in **Table 5.** A total of 79 subjects (25.0%) were reported to be symptomatic. All subjects were high-risk for carotid endarterectomy, with 159 subjects (50.3%) being high risk for anatomic reasons, 220 subjects (69.6%) for medical history (comorbidity) reasons. Sixty-three (63) subjects (19.9%) were high risk for both anatomic and comorbidity reasons. One hundred thirty-two (132/316, 41.8%) subjects were diabetics, 53.2% had a history of coronary artery disease, 24.7% a history of MI and 24.1% had COPD. A vast majority of patients had hypertension (93%) and dyslipidemia (90%). Fourteen (14) subjects had a history of atrial fibrillation (AF). Of these 14, three (3) subjects had ongoing AF at the time of enrollment.

TABLE 5: PATIENT MEDICAL HISTORY

Subject Medical History	ITT (N = 316)
Alzheimer's Disease	0.0% (0/316)
Diabetes Mellitus	41.8% (132/316)
Angina	21.2% (67/316)
Cardiac Arrhythmia	10.1% (32/316)
Atrial Fibrillation	4.4% (14/316)
Congestive Heart Failure	7.0% (22/316)
Chronic Obstructive Pulmonary Disease	24.1% (76/316)
Coronary Artery Disease	53.2% (168/316)
Previous PCI	33.9% (107/316)
Hypercholesterolemia / Dyslipidemia	89.9% (284/316)
Hypertension	93.0% (294/316)
Peripheral Vascular Disease	30.1% (95/316)
Myocardial Infarction	24.7% (78/316)
Stroke	22.2% (70/316)
Transient Ischemic Attack	13.0% (41/316)
Amaurosis Fugax	13.3% (42/316)
Previous Carotid Intervention at the target vessel	5.1% (16/316)
Symptomatic	25.0% (79/316)

Subject Medical History	ITT (N = 316)
High risk for CEA	100% (316/316)
High risk for CEA due to anatomic condition	50.3% (159/316)
High risk for CEA due to comorbidity	69.6% (220/316)
High risk for CEA due to both conditions	19.9% (63/316)

iii. Lesion Characteristics

Lesion characteristics as determined by an independent core lab are summarized in **Table 6** below. The mean lesion length was 18.6 mm, with moderate to severe calcification reported in approximately 35% of them. The mean pre-procedure target lesion percent stenosis was 90.2%.

TABLE 6: LESION CHARACTERISTICS (CORE LAB)

Lesion Characteristics	ITT (N = 316)*
Target Lesion Side	
Left	51.0% (159/312*)
Right	49.0% (153/312)
Calcification#	
None/Mild	64.3% (200/311**)
Moderate	20.6% (64/311)
Severe	15.1% (47/311)
Lesion length (mm)	
N	308***
Mean ± SD	18.6 ± 7.3
Median	18.0
Min, Max	2.2, 44.1
Minimum Lumen Diameter (mm)	
N	308
Mean ± SD	1.0 ± 0.6
Median	0.9
Min, Max	0.1, 3.2
Reference Lumen Diameter (mm)	
N	308
Mean ± SD	4.0 ± 0.7
Median	4.0
Min, Max	1.0, 6.8
Stenosis (%)	
N	311
Mean ± SD	90.2 ± 9.7
Median	93.0
Min, Max	53.0, 100.0

*Four (4) ITT subjects did not have Core Lab target lesion side reported,
**One (1) additional patient also did not have calcification and stenosis reported and
***An additional three (3) subjects did not have lesion length, minimum lumen diameter and reference lumen diameter reported.
#Two views were used to assess calcification. In the event that the two views reported different calcification, the most severe calcification were reported. Calcification Scoring System: None/Mild: No visualized radiopacities noted in target lesion (TL) / Moderate: Radiopacities noted in TL that are non-circumferential / Severe: Radiopacities noted in TL that are circumferential.

iv. Procedure Characteristics

A summary of procedure outcomes is provided in **Table 7**. The mean residual stenosis at the completion of the study procedure was 7.2%. At least half of the lesions had 0% stenosis at the end of the procedure (median = 0%). Embolic protection of the target vessel was mandatory per protocol (100% performed). Preclinical testing supported the compatibility of the CGuard Prime Stent System with either the Emboshield NAV6 or Mo.Ma embolic protection devices (EPDs). The clinical protocol allowed for the investigator to choose between these two EPD options. Some investigators chose to use two (i.e., both Emboshield Nav 6 and Mo.Ma Ultra) Embolic Protection Devices (EPDs) during the procedure per their common practice. Emboshield NAV6 alone was used in 237 subjects, 54 subjects had Mo.Ma Ultra alone, 24 subjects had Emboshield NAV6 and Mo.Ma used together, and

a non-study EPD (Filterwire EZ) was used for one subject due to the unavailability of any of the protocol required EPD at the time of procedure. Three (3) subjects received a non-study stent, while six (6) other subjects were implanted with 2 study stents.

TABLE 7: PROCEDURAL CHARACTERISTICS

Procedural Characteristics	**ITT (N = 316)**
Balloon Pre-dilation Performed	
No	7.0% (22/316)
Yes	93.0% (294/316)
Balloon Post-dilation Performed	
No	3.2% (10/316)
Yes	96.8% (306/316)
Embolic Protection Device*	**100.0% (316/316)**
Emboshield NAV6 alone	75.0 (237/316
Mo.Ma Ultra alone	17.1% (54/316)
Both EPDs	7.6% (24/316)
Non-study EPD	0.3% (1/316)
Post-procedure stenosis (%)	
N	302
Mean ± SD	7.2 ± 11.9
Median	0.0
Min, Max	0.0, 62.0
Study stents implanted	**319**
Size 8x30 mm	27/319 (8.6%)
Size 9x30 mm	38/319 (12.1%)
Size 10x30 mm	63/319 (20.1%)
Size 8x40 mm	41/319 (13.1%)
Size 9x40 mm	53/319 (16.9%)
Size 10x40 mm	97/319 (31.0%)
Non-study stents implanted	**3**
More than one study stent implanted	**6**

D Safety and Effectiveness Results

i. Primary Safety and Effectiveness Results

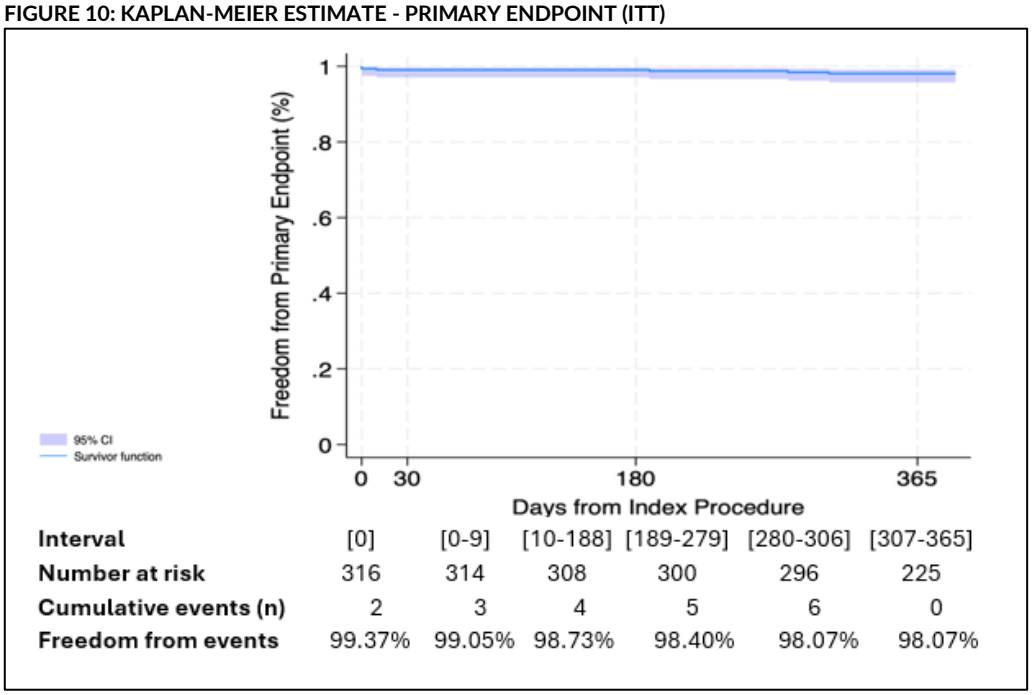
The primary analysis of safety and effectiveness was based on the ITT population of 316 subjects with 300 patients with evaluable primary endpoint information through 1 year. The primary endpoint was defined as the incidence of the following Major Adverse Events: Death (all-cause mortality), all Stroke, and Myocardial Infarction (DSMI) through 30-days post-index procedure, or ipsilateral stroke between 31 and 365 days. All primary endpoint events were adjudicated by the study independent Clinical Event Committee (CEC).

Three (3) subjects (0.95%) had one or more MAEs through 30 days post-index procedure. Of those MAEs, two (2) were due to a minor stroke, and one (1) was due to a major stroke and resulted in death at day 10 in a subject who stopped DAPT, a major protocol deviation. Three (3) subjects (1.00%) had an ipsilateral stroke between 31- and 365-days post-index procedure. Of those, two (2) were major and one (1) was minor.

The binary MAE proportion at 1-year was 2.00% (6/300). The corresponding one-sided 95% upper confidence limit (UCL) for the MAE proportion was 4.3%, substantially lower than the pre-specified performance goal of 11.6%. The binomial test of the binary MAE proportion versus the 11.6% performance goal produced a significant one-sided p value < 0.001, leading to the conclusion of study success. The binary MAE proportions were concordant in the mITT and PP populations, with MAE rates through 1-year of 2.00% and 1.75%, respectively. No hypothesis testing was performed on the mITT or PP populations.

Pre-specified Kaplan-Meier estimates analyses were performed for the primary endpoint. No hypothesis testing was performed. Following the index procedure, 98.06% of treated patients were free of death, stroke or MI (DSMI) at 30 days or ipsilateral stroke between 31 and 365 days in the ITT population. The Kaplan-Meier estimate for the primary endpoint rate is 1.93% in the ITT population (**Figure 10**). The Kaplan-Meier estimates in the mITT and PP populations were comparable at 1.94% and 1.71%, respectively.

FIGURE 10: KAPLAN-MEIER ESTIMATE - PRIMARY ENDPOINT (ITT)



Kaplan-Meier curve shows freedom from perioperative composite and ipsilateral stroke between 31 days and 1 year. The overall composite event-free rate is 98.07% at 1year. Brackets denote the beginning and end of intervals. Number at risk represents the number of patients at risk of events at the end of each interval. Number of events are cumulative.

ii. Secondary Endpoints Results

Secondary endpoint results were descriptive in nature without any formal statistical hypotheses testing.

Major Adverse Event (MAE) Rates

Table 8 and **Table 9** present the cumulative individual MAE number of events and rates through discharge, 30-day, 6-month and 1-year, as well as the rates for each individual MAE and for the composite of DSMI at the same timepoints in the ITT and PP populations, respectively.

TABLE 8: MAE COMPOSITE RATE (DSMI) AND INDIVIDUAL RATES (ITT)

	ITT Population N=316)			
MAE	**Discharge**	**30-day**	**180-day**	**1-year**
	n/N (%)	**n/N (%)**	**n.N (%)**	**n/N (%)**
Death, Stroke, MI	2/316 (0.6%)	3/316 (0.9%)	5/316 (1.6%)	15/316 (4.7%)
Death (all cause)	0	1/316 (0.3%)	1/316(0.3%)	7/316 (2.2%)
Stroke	2/316 (0.6%)	3/316 (0.9%)	5/316 (1.6%)	9/316 (2.8%)
Myocardial Infarction	0	0	0	0
Ipsilateral Stroke	1/316 (0.3%)	2/316 (0.6%)	2/316 (0.6%)	5/316 (1.5%)
Major Ipsilateral Stroke	0	1/316 (0.3%)	1/316 (0.3%)	3/316 (0.9%)

TABLE 9: MAE COMPOSITE RATE (DSMI) AND INDIVIDUAL RATES (PP)

	PP Population (N=295)			
MAE	**Discharge**	**30-day**	**180-day**	**1-year**
	n (%)	**n (%)**	**n (%)**	**n (%)**
Death, Stroke, MI	2/295 (0.7%)	2/295 (0.7%)	3/295 (1.0%)	12/295 (4.1%)
Death (all cause)	0	0	0	5 (1.7%)
Stroke	2/295 (0.7%)	2/295 (0.7%)	3/295 (1.0%)	7/295 (2.4%)
Myocardial Infarction	0	0	0	0
Ipsilateral Stroke	1/295 (0.3%)	1/295 (0.3%)	1/295 (0.3%)	4/295 (1.4%)
Major Ipsilateral Stroke	0	0	0	2/295 (0.7%)

Kaplan-Meier estimates for these time-to-event endpoints yielded similar results. At 1-year the K-M estimates for the ITT and PP populations are as follow (**Table 10**):

TABLE 10: K-M ESTIMATES FOR MAE COMPONENT RATES THROUGH 1-YEAR (ITT AND PP)

K-M estimates	ITT	PP
Death (all cause)	2.3%	1.7%
Stroke	2.9%	2.4%
Myocardial Infarction	0	0
Ipsilateral Stroke	1.6%	1.4%

Sensitivity Analyses

Tipping point analysis

A tipping point analysis using the ITT population for the primary endpoint was performed, where patients with missing data are considered failures, one at a time, until the primary endpoint null hypothesis is not rejected. Using a binomial test, the tipping point sensitivity analysis demonstrated that the primary endpoint outcomes were robust with a value of 6.96% (22/316) with a 95% CI of (4.41%, 10.35%), as shown in Table 11. Even with all missing data considered as failure, the null hypothesis was rejected.

TABLE 11: TIPPING POINT ANALYSIS (ITT)

	Proportion (n/N), 95% CI	Binomial test p-value
Primary Endpoint – missing data imputed as failure	6.96% (22/316), (4.41%, 10.35%)	0.005

Sensitivity analysis using the UDMI for periprocedural MI events

A sensitivity analysis was performed using the UDMI for periprocedural MI events, for primary objective analysis and for the first two secondary objective analyses that involve DSMI endpoints. There was no difference in outcome of the primary endpoint when using the UDMI definition of MI in the analysis.

Multiple imputations

For the primary analysis, missing data was imputed using multiple imputation methods. A total of 50 imputations were carried out for the primary endpoint. The imputed primary endpoint rate in the ITT population was 2.39%, with an upper bound 95% CI of 4.25%, well below the Performance Goal of 11.6%.

Poolability of Sites

Consistency of the primary endpoint between sites with 5 or more subjects was evaluated using the Fisher's exact test resulting in a p-value = 0.4865. Data from sites was therefore considered poolable.

In-stent restenosis through 1-year as determined by Core Laboratory

Incidence of in-stent Restenosis (ISR) is determined via transcervical duplex ultrasound imaging assessed by the Core Laboratory. ISR > 70% is defined as PSV > 300 cm/s associated with stent, or vessel occlusion, and ISR > 50% is defined as PSV > 220 cm/s associated with stent, or vessel occlusion. The percent diameter stenosis at 1-year is summarized in **Table 12**. For those subjects with a 1-year image, 7.0% had >50% stenosis and 2.5% had >70% restenosis in the mITT population (implanted with the study stent).

TABLE 12: IN-STENT RESTENOSIS (MITT) PER CORE LABORATORY AT 1-YEAR

	mITT (N = 313) Proportion (n/N, (95% CI)
In-Stent Restenosis > 70%	2.5% (7/284*), (1.0%, 5.0%)
Symptoms associated with restenosis	0.4% (1/284), (0.0%, 1.9%)
In-Stent Restenosis > 50%	7.0% (20/284), (4.4%, 10.7%)
Symptoms associated with restenosis	0.4% (1/284), (0.0%, 1.9%)
Vessel Occlusion	0.7% (2/292**), (0.1%, 2.5%)

*The denominator of 284 includes those mITT subjects that had a core lab-reported maximum peak systolic velocity (PSV and available stent patency at one-year.

**Vessel occlusion is based on stent patency available at one-year.

Target Lesion Revascularization (TLR) through 1-year

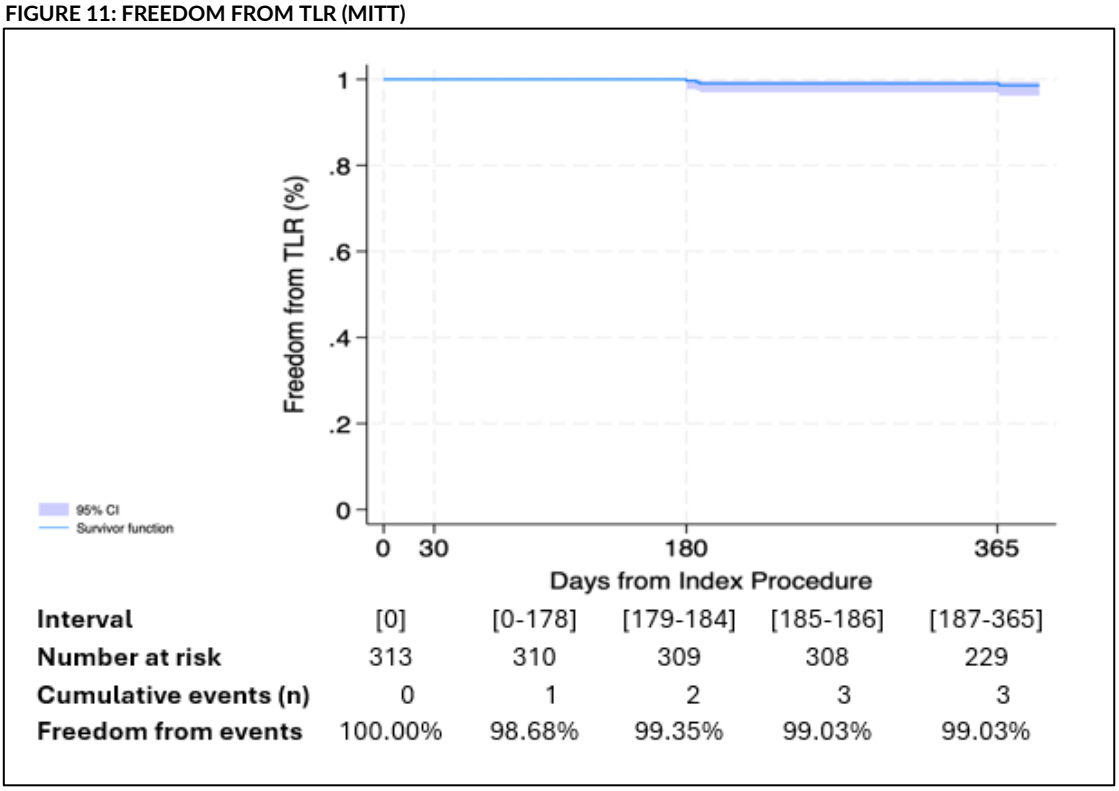
TLR was defined in the protocol as revascularization procedure of the original treatment site, including angioplasty, stenting, endarterectomy, or thrombolysis, performed to open or increase the luminal diameter within the stented lesion or within 5 mm proximal or distal to the index stent.

Clinically driven Target Lesion Revascularization (CD-TLR) was further defined as any surgical or percutaneous revascularization of the target lesion and associated with symptoms (amaurosis fugax, transient ischemia attack (TIA) or stroke ipsilateral to the side of the stenosis) or a narrowing of >80% using NASCET criteria by Core lab. This includes repeat angioplasty, stenting, endarterectomy or extracranial-intracranial bypass.

Three (3) patients were adjudicated as having a TLR during the one-year period in the mITT population. Subjects were required to either have an event of interest (TLR) within one-year or at least 335 days of follow-up to be included in the analysis. The binary TLR rate at 1-year was 1.0% (3/299) with a 95% CI (0.2%, 2.9%). All 3 subjects were treated with a non-study stent placed within the study stent. All 3 TLR subjects were asymptomatic, but Core lab angiographic results revealed a >80% stenosis for one subject CG-001-035, meeting the definition of CD-TLR. The overall CD-TLR rate at 1-year was 0.3% (1/299).

Freedom from TLR at 1-year by Kaplan-Meier Analysis was 99.03% in the mITT population **Figure 11**.

FIGURE 11: FREEDOM FROM TLR (MITT)



Interval	[0]	[0-178]	[179-184]	[185-186]	[187-365]
Number at risk	313	310	309	308	229
Cumulative events (n)	0	1	2	3	3
Freedom from events	100.00%	98.68%	99.35%	99.03%	99.03%

Kaplan-Meier curve shows freedom from TLR between procedure day and 1 year. The overall event-free rate is 99.37% at 1 year. Brackets denote the beginning and end of intervals. Number at risk represents the number of patients at risk of events at the end of each interval. Number of events are cumulative.

Prespecified Site Reported Device Related Events Discharge through 1-year
Incidences of ipsilateral stroke (e.g., major and minor), stent thrombosis, cardiovascular death as adjudicated by the CEC, and other pre-specified device related clinical events as reported by the sites, are summarized for the ITT population in **Table 13**.

TABLE 13: PRESPECIFIED CEC AND SITE REPORTED DEVICE RELATED EVENTS THROUGH 1-YEAR

	ITT (N= 316)	
	AEs (n)	**Subjects n (%), (95% CI)**
Adjudicated by CEC		
Ipsilateral Stroke	4	4 (1.3%), (0.3%, 3.2%)
Stent Thrombosis	1*	1 (0.3%), (0.0%, 1.8%)
Cardiovascular Death	3	3 (0.9%), (0.2%, 2.7%)
Site reported		
Other Device Related Events		
Carotid artery occlusion	1*	1 (0.3%), (0.0%, 1.8%)
Carotid artery stenosis	1	1 (0.3%), (0.0%, 1.8%)
Claudication of jaw muscles	1	1 (0.3%), (0.0%, 1.8%)
Dysarthria	1	1 (0.3%), (0.0%, 1.8%)
Headache	1	1 (0.3%), (0.0%, 1.8%)
Neck pain	1	1 (0.3%), (0.0%, 1.8%)
Pain in jaw	1	1 (0.3%), (0.0%, 1.8%)
Vascular Stent occlusion*	2	2 (0.3%), (0.0%, 1.8%)
Vascular Stent stenosis	3	3 (0.9%), (0.0%, 1.8%)

*This subject is counted twice in Table 13 as a site-reported carotid artery occlusion and as an adjudicated stent thrombosis by the CEC.

Technical and Treatment Success

Technical Success was defined as the number of subjects with at least one CGuard Prime device successfully delivered and deployed with final residual diameter stenosis <30% based on quantitative angiography measurements at the end of the index procedure. Technical success was achieved in 91.7% of the ITT population (278/303); twenty-two (22) failures to achieve technical success were due to final diameter residual stenosis ≥30% and three (3) to non-deployment (**Table 14**).

The CGuard Prime Treatment Success was defined as the number of subjects with Technical Success and who did not experience any Major Adverse Event based on CEC adjudication through 30 Days. Treatment Success was achieved in 90.8% (275/303) of the ITT population as three (3) subjects experienced a stroke within 30 days, one of which was adjudicated as a major ipsilateral stroke and death (**Table 14**).

TABLE 14: CGUARD PRIME TECHNICAL AND TREATMENT SUCCESS

	ITT (N = 316) **Proportion (n/N),** **(95% CI)**	**Per Protocol (N = 295)** **Proportion (n/N),** **(95% CI)**
Technical Success	91.7% (278/303*), (88.1%, 94.6%)	93.0% (264/284**), (89.3%, 95.6%)
Treatment Success	90.8% (275/303*), (86.9%, 93.8%)	92.3% (262/284**), (88.5%, 95.1%)

*Post-intervention imaging to determine stenosis percent was not available from the core lab for 13 ITT subjects.
These subjects were not included in the assessment of technical and treatment success.
** Post-intervention imaging to determine stenosis percent was not available from the core lab for 11 PP subjects.
These subjects were not included in the assessment of technical and treatment success.

Post-Hoc Analysis

As a post-hoc analysis, the sponsor performed an analysis of technical success defined as the number of subjects with at least one CGuard Prime device successfully delivered and deployed with final residual cross-sectional stenosis <50% based on quantitative angiography measurements at the end of the index procedure as assessed by the Core Lab, divided by the number of patients with attempted implant of the CGuard stent in the ITT population. Technical success was achieved in 98.3% of the ITT population (298/303); two failures to achieve technical success were due to final residual stenosis ≥50% and three to non-deployment.

Treatment Success, per the post-hoc analysis, rate was achieved in 97.4% (292/303) of the ITT population as three (3) subjects experienced a stroke within 30 days, one of which was adjudicated as a major ipsilateral stroke and death (**Table 15)**.

TABLE 15: POST HOC. CGUARD PRIME TECHNICAL AND TREATMENT SUCCESS

	ITT (N = 316) Proportion (n/N), 95% CI	**Per Protocol (N = 295) Proportion (n/N), (95% CI)**
Technical Success	98.3% (298/303*), (96.2%, 99.5%)	99.3% (282/284**), (97.5%, 99.9%)
Treatment Success	97.4% (295/303*), (94.9%, 98.9%)	98.6% (280/284**) (96.4%, 99.6%)

*Post-intervention imaging to determine stenosis percent was not available from the core lab for 13 ITT subjects.
These subjects were not included in the assessment of technical and treatment success.
**Post-intervention imaging to determine stenosis percent was not available from the core lab for 11 PP subjects.
These subjects were not included in the assessment of technical and treatment success.

iii. Adverse Events

An Adverse Event (AE) was defined as 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 and whether anticipated or unanticipated. (ISO 14155:2020)

A Serious Adverse Event (SAE) was defined as Adverse Event that led to any of the following:

1. Death
2. Serious deterioration in the health of the subject, users, or other persons as defined by one or more of the following:
    a. a life-threatening illness or injury
    b. a permanent impairment of a body structure or a body function, including chronic disease, or
    c. in-patient or prolonged of an existing hospitalization, or
    d. Resulted in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function, fetal distress, fetal death, a congenital abnormality, or birth defect including physical or mental impairment. (ISO 14155:2020).

A planned hospitalization for a pre-existing condition was not considered a SAE. An Adverse Device Effect (ADE) was defined as an Adverse Event related to use of an investigational medical device.

An Unanticipated Adverse Device Effect (UADE) means 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 (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects. (21CFR 812.3)

An Unanticipated Serious Adverse Device Effect (USADE) is defined as a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report. (ISO 14155:2020)

As shown in **Table 16**, of the 316 subjects, 115 (36.4%) subjects experienced an adverse event through the 30-day follow-up, and 193 (61.1%) subjects experienced an adverse event through the 12-month follow-up. Thirty-seven (37) subjects (11.7%) experienced a serious adverse event through the 30-day follow-up, and 102 (32.3%) subjects experienced a serious adverse event through the 12-month follow up. No unexpected adverse device events (UADE) or unexpected serious adverse device events (USADE) were observed in any subject.

Table 16 summarizes all AEs on or after the procedure through 365 days post-procedure (ITT).

TABLE 16: SUMMARY OF ALL AES ON OR AFTER THE PROCEDURE THROUGH 365 DAYS POST-PROCEDURE (ITT)

System Organ Class Preferred Term	**Number of events**	**Number (%) of Subjects**
Total	**497**	**193 (61.1%)**
Blood and lymphatic system disorders	**7**	**7 (2.2%)**
Anaemia	6	
Leukocytosis	1	
Cardiac disorders	**72**	**49 (15.5%)**
Acute myocardial infarction	14	
Atrial fibrillation	11	
Bradycardia	14	
Coronary artery disease	10	
Palpitations	4	
Eye disorders	**11**	**8 (2.5%)**
Vision blurred	4	
Gastrointestinal disorders	**20**	**16 (5.1%)**
General disorders and administration site conditions	**23**	**20 (6.3%)**
Chest pain	10	
Vascular stent stenosis	4	
Infections and infestations	**61**	**43 (13.6%)**

System Organ Class Preferred Term	Number of events	Number (%) of Subjects
COVID-19	9	
Cellulitis	4	
Influenza	4	
Pneumonia	6	
Urinary tract infection	9	
Injury, poisoning and procedural complications	**42**	**38 (12.0%)**
Fall	4	
Post procedural hypotension	10	
Investigations	**11**	**10 (3.2%)**
Troponin increased	4	
Metabolism and nutrition disorders	**12**	**10 (3.2%)**
Hypokalaemia	4	
Musculoskeletal and connective tissue disorders	**22**	**16 (5.1%)**
Neck pain	5	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**10**	**10 (3.2%)**
Nervous system disorders	**66**	**50 (15.8%)**
Carotid artery stenosis	18	
Dizziness	5	
Headache	6	
Syncope	7	
Renal and urinary disorders	**14**	**14 (4.4%)**
Acute kidney injury	8	
Respiratory, thoracic and mediastinal disorders	**13**	**13 (4.1%)**
Skin and subcutaneous tissue disorders	**8**	**7 (2.2%)**
Surgical and medical procedures	**7**	**7 (2.2%)**
Vascular disorders	**86**	**73 (23.1%)**
Hypertension	8	
Hypotension	43	
Peripheral artery occlusion	4	
Peripheral vascular disorder	7	

System organs with a total rate of aggregated AEs and individual AEs with <1% prevalence are not displayed.

Examination of Subgroups

The primary endpoint rate and its two-sided exact 95% confidence interval is presented within each of the following subgroups in Table 17. The purpose of these subgroup analyses is to assess consistency of results across subgroups. Although differences between groups can be noted, all Confidence Intervals (CI) overlap between subgroups.

TABLE 17: SUBGROUP ANALYSIS FOR PRIMARY ENDPOINT (ITT)

Category / Subgroup	Primary Endpoint (%, n/N)	95% CI
Sex		
Male	2.6% (5/191)	(0.9%, 6.0%)
Female	0.9% (1/109)	(0.0%, 5.0%)
Age		
Below the median (70.0)	3.6% (5/139)	(1.2%, 8.2%)
Above the Median (70.0)	0.6% (1/161)	(0.0%, 3.4%)
Race / Ethnicity		
Caucasian	2.1% (6/292)	(0.8%, 4.4%)
Non-Caucasian	0.0% (0/8)	(0.0%, 36.9%)
Symptomatic Status		
Symptomatic	6.8% (5/74)	(2.2%, 15.1%)
Asymptomatic	0.4% (1/226)	(0.0%, 2.4%)

Post-hoc Subgroup Analyses for CGuard Prime

The CGuard Prime Carotid Stent System was introduced in the last phase of the study and was implanted in 32 patients. The CGuard and CGuard Prime Carotid Stent Systems are the same implantable stent and only differ in their delivery system and handles. A post hoc analysis was conducted on the primary endpoint for only those subjects who received a CGuard Prime device as shown in **Table 18.** A post hoc analysis was performed on the same group using the pre-specified definitions of technical and treatment success endpoints (i.e., final residual diameter stenosis <30%) (**Table 19**).

TABLE 18: POST HOC. PRIMARY ENDPOINT (CGUARD PRIME)

	CGuard Prime (N = 32) Proportion (n/N), 95% CI
Primary Endpoint	0.00% (0/27), (0.00%, 12.77%)
MAE through 30 Days	0.00% (0/32), (0.00%, 10.89%)
Death (all cause)	0.00% (0/32), (0.00%, 10.89%)
Stroke	0.00% (0/32), (0.00%, 10.89%)
Myocardial Infarction*	0.00% (0/32), (0.00%, 10.89%)
Ipsilateral Stroke Days 31-365	0.00% (0/27), (0.00%, 12.77%)

Table is hierarchical. Only the first occurring event that meets the definition of one of the components is presented.
*Classified based on the ARC2 definition

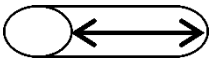
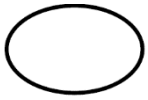
TABLE 19: POST HOC. TECHNICAL AND TREATMENT SUCCESS (CGUARD PRIME VS CGUARD) (ITT)

	CGuard Prime (N = 32) Proportion (n/N), 95% CI	**CGuard (N = 284) Proportion (n/N), 95% CI**
Technical Success	93.8% (30/32), (79.2%, 99.2%)	91.5% (248/271), (87.5%, 94.5%)
Treatment Success	93.8% (30/32), (79.2%, 99.2%)	90.4% (245/271), (86.3%, 93.6%)

These post-hoc subgroup analyses were not powered to detect differences between CGuard and CGuard Prime Carotid Stent Systems. 95% CIs overlap substantially and show no evidence of a difference in technical, treatment success or in the primary endpoint (or its components) between CGuard and CGuard Prime Carotid Stent Systems.

Pediatric Extrapolation
In this premarket application, existing clinical data were not leveraged to support approval of a pediatric patient population.

SYMBOL DEFINITIONS

	CAUTION		USE BY DATE
	KEEP AWAY FROM SUNLIGHT		STERILIZED WITH ETHYLENE OXIDE GAS
	CATALOG NUMBER		DO NOT REUSE
	KEEP DRY		DO NOT RESTERILIZE
	SERIAL NUMBER		DO NOT USE IF PACKAGE IS DAMAGED
	TEMPERATURE LIMITATION		CONSULT INSTRUCTIONS FOR USE
	MR conditional		STENT LENGTH
	MANUFACTURER		COUNTRY OF MANUFACTURE
	SINGLE STERILE BARRIER SYSTEM		SINGLE STERILE BARRIER SYSTEM WITH PROTECTIVE PACKAGING OUTSIDE
	UNIQUE DEVICE IDENTIFIER		MEDICAL DEVICE
	INNER DIAMETER		OUTER DIAMETER
	MODEL NUMBER		PACKAGING UNIT
	CAUTION: FEDERAL LAW RESTRICTS THIS DEVICE TO SALE BY OR ON THE ORDER OF A PHYSICIAN		

InspireMD Ltd.
4 Menorat Hamaor Street
Tel Aviv, 6744832 Israel
Phone: +972-3-6917691

US Headquarters:
InspireMD Inc.
6303 Waterford District Dr.
Suite 215
Miami, FL 33126
1-786-425-3292

Date of Issue: 2025-03-14