PRO-Kinetic Energy

Cobalt Chromium (CoCr) Coronary Stent System

English

STERILE EO

Caution: Federal law restricts this device to sale by or on the order of a physician.

BIOTRONIK
excellence for life

Device Description

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System consists of a balloon- expandable stent (1) pre-mounted on a fast-exchange delivery system. The stent is intended as a permanent implant. It is made from a cobalt chromium alloy (L-605) and is coated with a thin layer of amorphous silicon carbide (proBIO). There are two different stent designs: small (2.25 – 3.0 mm stent inner diameter) and medium (3.5 – 4.0 mm stent inner diameter). See Table 1 "Stent Parameters" for stent characteristics. The delivery system is a fast-exchange PTCA catheter with a working length of 140 cm. To facilitate fluoroscopic visualization and positioning, the stent is centered between two radiopaque markers (2a and 2b). The proximal shaft of the stent system is a polymer covered hypotube (3). It has a single Luer port (4) for connecting an inflation/deflation device to inflate/deflate the balloon (5). The catheter has a hydrophobic coating on the outer surface of the proximal shaft and a hydrophilic coating on the outer surface of the distal shaft. The guide wire lumen (6) starts at the delivery system tip (7) and ends at the guide wire exit port (8), 29 cm from the distal end. The stent system is compatible with guide wires (9) of 0.014" (0.36 mm) diameter and guiding catheters with an inner diameter of ≥ 0.056" (1.42 mm). To indicate when the delivery system tip exits from the guiding catheter, shaft exit markers are located on the hypotube 92 cm (10a) (brachial technique) and 102 cm (10b) (femoral technique) from the distal end of the delivery system. To facilitate handling of the stent system, the hub (11) has a "click-in" hypotube fastener (12) that can be used when the stent system is stored on the preparation table.

Caution: This fastener is intended to hold only the hypotube section of the delivery system; the distal shaft should not be held by the "click-in" fastener.

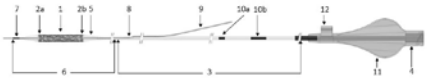

Table 1: Stent Parameters

Stent Parameters						
	Stent Inner Diameter (mm)					
Stent Design	SMALL				MEDIUM	
Nominal strut thickness	60µm				80µm	
Percent stent free area	82%	84%	86%	87%	88%	89%
Stent length (mm)	2.25	2.50	2.75	3.0	3.5	4.0
9	x	x	x	x	x	x
13	x	x	x	x	x	x
15	x	x	x	x	x	x
18	x	x	x	x	x	x
20	x	x	x	x	x	x
22		x	x	x	x	x
26			x	x	x	x
30			x	x	x	x
35					x	x
Nominal distance between radiopaque marker and stent	0.3 mm					
Maximum expandable diameter *	3.50 mm				4.65 mm	
*If post-dilation is required, DO NOT post-dilate the stent more than the maximum expandable diameter.						

How Supplied

STERILE. Non-pyrogenic. Device is sterilized with ethylene oxide. DO NOT use if the package is opened or damaged, or if any information provided is obscured or damaged.

Contents

- One (1) PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System and one (1) Compliance Chart in a sealed, peel-open pouch.
- One (1) Patient Implant Card

Storage

Store in a cool, dry, dark place.

Indications

The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System is indicated for improving coronary luminal diameter in patients with de novo or restenotic lesions in native coronary arteries with a reference vessel diameter ranging from 2.25 mm to 4.0 mm and lesion length ≤ 31 mm.

Contraindications

Contraindications for the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System include, but are not limited to:

- Patients with a known hypersensitivity or allergy to stent coating materials (amorphous silicon carbide) or to L-605 CoCr alloy (cobalt, chromium, tungsten, nickel).
- Patients with a known severe reaction to contrast agents that cannot be adequately pre-medicated prior to the stent placement procedure.

Coronary artery stenting is contraindicated for use in the following:

- Patients who are contraindicated for antiplatelet and/or anticoagulation therapy.
- Patients who are judged to have a lesion that prevents complete inflation of an angioplasty balloon.

Warnings

- Device is supplied STERILE and for single use only. DO NOT re-sterilize and/or reuse. Reuse of single use devices creates potential risks including infections. Contamination of the device may lead to serious injury or patient harm.
- DO NOT use if the sterile package is opened or damaged or any information provided is obscured.
- DO NOT use after the "use by" date specified on the label.
- DO NOT attempt to remove or readjust the stent on the delivery system. The stent cannot be removed and placed on another balloon catheter.
- DO NOT expose the stent system to organic solvents, e.g. alcohol.
- Appropriate anticoagulation and antiplatelet therapy should be administered pre- and post-procedure in accordance with standard practices.
- When the stent system is in the body, it should be manipulated while under high quality fluoroscopy.
- DO NOT rotate the system if the tip is constrained.
- It is only recommended to place overlapping stents using two PRO-Kinetic Energy Cobalt-Chromium Bare Metal stents. The risk of corrosion increases when stents of differing metals contact one another.
- To reduce the potential for vessel damage, the inflated diameter of the balloon should NEVER exceed the original diameter of the vessel proximal and distal to the lesion.
- Balloon pressure should not exceed the Rated Burst Pressure (RBP). Use of a pressure-monitoring device is mandatory to prevent over-pressurization.
- Use only an appropriate balloon inflation medium (e.g. 50:50 mixture by volume of contrast medium and saline). NEVER use air or any gaseous medium to inflate the balloon.
- Subsequent restenosis may require repeat dilatation of the arterial

segment containing the stent. The long-term outcomes following repeat dilatation of endothelialized stents are unknown.

Precautions

- Only physicians thoroughly trained and educated in the performance of percutaneous coronary intervention (PCI) should use this device.
- Prior to the procedure, the stent system should be visually examined to verify functionality and ensure that its size is suitable for the specific procedure for which it is to be used.
- PTCA and stent implantation should only be performed at medical facilities where procedures can be readily performed in the event of a potential injury or life-threatening complication.
- Exercise care during handling to reduce the possibility of disrupting the placement of the stent on the balloon, accidental breakage, bending or kinking of the delivery system.
- Use only guide wires with a maximum diameter of 0.014" (0.36 mm).
- Use guiding catheters with a minimum inner diameter of ≥0.056" (1.42 mm).
- Ensure that the guide wire exit port remains inside the guiding catheter at all times. Guide wire exit port is indicated on the label.
- The use of mechanical atherectomy devices or laser catheter is not recommended within the stented area.
- The hypotube fastener is intended to hold only the hypotube section of the delivery system; the distal shaft should not be held by the "click-in" fastener.
- Stent retrieval methods (use of additional wires, snares and/or forceps) may result in additional trauma to the coronary vasculature and/or the vascular access site. Complications can include bleeding, hematoma or pseudoaneurysm.
- Narrow, calcified and tortuous lesions or other lesions that could impede the delivery of the stent must be pre-dilated with an appropriately sized angioplasty balloon or pre-treated with an appropriately sized angioplasty balloon or pre-treated with another method before using the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System.
- Take care when removing the stent system from the protection ring as forceful movements may dislocate the protector and the stent.
- When removing the stent protector, always pull at the very distal end of the protector to avoid dislocation of the stent.
- Avoid excessive manipulation of the stent during flushing of the guide wire lumen.
- DO NOT apply negative pressure to the stent system at any time prior to placement of the stent across the lesion. This may cause loosening and dislodgement of the stent.
- When inserting and positioning the stent system, ensure that the hemostatic valve of the guiding catheter is fully open. A partially opened hemostatic valve might damage the stent or dislodge it from the centered location on the balloon.
- DO NOT apply excessive force while accessing or crossing the lesion. This may damage the stent and / or dislodge it from the balloon. If resistance is felt at any time, stop the procedure and determine the cause of resistance before proceeding. If the stent system is unable to reach or cross the lesion easily, the procedure should be aborted. In this case, follow the instruction for the "Removal of an unexpanded stent".
- DO NOT inflate the balloon if a vacuum cannot be held, as this indicates a leak in the delivery system. If a vacuum cannot be held follow the instructions for the "Removal of an unexpanded stent".
- Inflate to at least the nominal pressure (NP) indicated on the label and the compliance chart. DO NOT exceed Rated Burst Pressure (RBP).
- Avoid barotrauma outside the stent margins during post-dilatation.
- DO NOT post-dilate the stent to more than the maximum expandable diameter recommended in Table 1: "Stent Parameters".
- Exercise care when crossing a newly deployed stent with a coronary guide wire, balloon catheter or stent system to avoid disruption of the stent geometry and stent migration.
- If resistance is encountered at any time during removal of the system, follow the instructions for the "Removal of the stent system / delivery system and the guiding catheter as a single unit."
- DO NOT RE-INSERT the stent system as the stent and / or the delivery system may have been damaged during the initial attempt to cross the lesion or during withdrawal.
- Failure to follow correct removal steps for an unexpanded stent system and / or applying excessive force to the stent system can potentially result in loss or damage to the stent and / or delivery system components.
- After use, dispose of the product and packaging in accordance with hospital, administrative and/or local government policy.

Potential Adverse Events / Complications

Possible adverse events / complications associated with PTCA and stent placement include, but are not limited to:

- Allergic reactions to contrast media, antiplatelet aggregation or anticoagulant medications, amorphous silicon carbide and / or L-605 CoCr (cobalt, chromium, tungsten and nickel).
- Arrhythmic events: Ventricular tachycardia, ventricular fibrillation, atrial fibrillation, bradycardia.
- Bleeding events: Access site bleeding or hemorrhage, hemorrhage requiring transfusion or other treatment
- Cardiac events: Myocardial infarction or ischemia, abrupt closure of coronary artery, restenosis of treated artery, cardiogenic shock, angina, tamponade, perforation or dissection of coronary artery or aorta, cardiac perforation, emergency cardiac surgery, pericardial effusion, aneurysm formation, cardiomyopathy.
- Death
- Infection and sepsis
- Neurologic events: Permanent (stroke) or reversible (TIA) neurologic event, femoral nerve injury, peripheral nerve injury.
- Renal events: renal insufficiency / renal failure.
- Respiratory events: Acute pulmonary edema, congestive heart failure, respiratory insufficiency or failure.
- Stent system events: Failure to deliver stent to intended site, stent dislodgement from the delivery system, stent misplacement, stent deformation, stent embolization, stent thrombosis or occlusion, stent fracture, stent migration, inadequate apposition or compression of stent/s, inflation difficulties, rupture or pinhole of the delivery system balloon, deflation difficulties, withdrawal difficulties, embolization of catheter material.
- Vascular events: Access site hematoma, hypotension / hypertension, pseudoaneurysm, arteriovenous fistula formation, retroperitoneal hematoma, vessel dissection or perforation, restenosis, thrombosis or occlusion, compromise of side branch patency, vasospasm, peripheral ischemia, dissection, distal embolization (air, tissue, debris, thrombus).

Pre- and Post- Procedure Antiplatelet Regimen

Dual antiplatelet and anticoagulation therapies should be administered according to the current medical guidelines. Post-procedure dual antiplatelet therapy compliance with the recommended medical guidelines is important, as early discontinuation could result in a higher risk of stent thrombosis, myocardial infarction or death.

Use of Multiple Stents

In the BIOHELIX-I clinical trial, the protocol specified that lesions were to be treated with no more than one stent, except in situations requiring bailout stenting. When more than one stent is required, overlapping stents should utilize stents of a similar composition to avoid the possibility of corrosion due to differing metals. The risk of corrosion increases when stents of differing metals contact one another.

Use in Special Populations

The safety and effectiveness of the PRO-Kinetic Cobalt-Chromium Bare Metal Energy Stent has not been evaluated in the following populations:

- Patients with vessel thrombus at the lesion site.
- Patients with coronary artery reference vessel diameter of less than 2.25 or greater than 4.0 mm.
- Patients with coronary artery lesions longer than 31 mm or requiring more than one stent.
- Patients with lesions located in saphenous vein grafts, in the left main coronary artery, ostial lesions or lesions located at a bifurcation.

- Patients with diffuse disease or poor flow distal to the identified regions.
- Patients with tortuous vessels (> 60 degrees) in the region of the obstruction or proximal to the lesion.
- Patients with recent acute myocardial infarction where there is evidence of thrombus or poor flow.
- Patients with in-stent restenosis.
- Patients with severe calcification in the lesion or total chronic occlusion.
- Patients with three vessel disease.

Directions for use

Patient preparation and stent system selection

01. Prepare the patient for a PCI procedure according to the institution's standard clinical practice.

Note: The crossing profile of the stent is printed on the label. The ability of the system to cross the lesion is limited by the crossing profile of the stent.

Caution: Narrow, calcified and tortuous lesions or other lesions that could impede the delivery of the stent must be predilated with an appropriately sized angioplasty balloon or pretreated with another method before using the PRO-Kinetic Energy Cobalt Chromium Coronary Stent System.

02. Select the stent size to match the diameter of the vessel to achieve a final stent diameter to vessel ratio of 1:1 and a full coverage of the lesion over its entire length.

Stent system preparation

Caution: Exercise care during device handling to reduce the possibility of disrupting the placement of the stent on the balloon and accidental breakage, bending or kinking of the stent system shaft.

03. Remove the protection ring containing the stent system from the sterile package and place it in a sterile field.

04. Remove the stent system from the protection ring.

Caution: Take care when removing the stent system from the protection ring, as forceful movements may dislocate the protector and the stent.

05. Carefully remove the balloon / stent protector.

Caution: When removing the stent protector, always pull at the very distal end of the protector to avoid dislocation of the stent.

06. Visually check the stent crimping for uniformity, no protruding struts, and centering on the balloon.

Pre-flush guide wire lumen

07. Connect a syringe containing sterile saline to an appropriately sized "flushing needle". Carefully apply the needle to the distal tip of the delivery system and flush the guide wire lumen.

08. Remove the syringe and the "flushing needle".

Caution: Avoid excessive manipulation of the stent during flushing of the guide wire lumen.

09. Leave the prepared stent system at ambient pressure.

Caution: DO NOT apply negative pressure to the stent system at any time prior to the placement of the stent across the lesion. This may cause loosening and dislodgement of the stent.

Insertion and stent positioning

10. Attach a hemostatic valve to the Luer-port of the guiding catheter positioned within the vasculature.

11. Position the guide wire under fluoroscopy in accordance with PCI techniques.

12. Back-load the proximal end of the guide wire into the distal tip of the delivery system until it exits at the guide wire exit port.

13. Open the hemostatic valve completely.

Caution: When inserting and positioning the stent system, ensure that the hemostatic valve of the guiding catheter is fully open. A partially opened hemostatic valve might damage the stent or dislodge it from the centered location on the balloon.

14. Carefully insert the stent system through the hemostatic valve.

15. Advance the stent system through the guiding catheter using fluoroscopic guidance to determine when the delivery system tip approaches the distal tip of the guiding catheter.

Note: The shaft exit markers on the hypotube may be used to approximate when the stent system has reached the distal end of the guiding catheter.

16. Carefully advance the stent system into the coronary artery over the guide wire while maintaining stable guiding catheter seating and stable guide wire placement across the target lesion.

17. Position the stent within the lesion using the balloon radiopaque markers as reference points.

Caution: DO NOT apply excessive force wile accessing or crossing the lesion. This may damage the stent and / or dislodge it from the balloon. If resistance is felt at any time, stop the procedure and determine the cause of resistance before proceeding. If the stent system is unable to reach or cross the lesion easily, the procedure should be aborted. In this case, follow the instructions for the "Removal of an unexpanded stent".

18. Verify the stent position via high resolution fluoroscopy to assure an adequate coverage of the lesion including the proximal and distal margins.

Remove air from the delivery system

19. Connect a three-way stopcock to the Luer-Lock of the catheter.

20. Prepare and remove air from a 20 ml capacity inflation/deflation device according to manufacturer's recommendations and instructions.

21. Attach the inflation/deflation device containing 3 ml of balloon inflation medium to the stopcock.

Warning: USE ONLY appropriate balloon inflation medium (e.g. 50:50 mixture by volume of contrast medium and saline). NEVER use air or any gaseous medium to inflate the balloon.

22. Open the stopcock so that an open fluid path between the catheter and the inflation/deflation device is established.

23. Pull the plunger of the inflation/deflation device and aspirate air from the catheter for at least 30 seconds.

Caution: DO NOT inflate the balloon if a vacuum cannot be held, as this indicates a leak in the delivery system. If a vacuum cannot be held, follow the instructions for the "Removal of an unexpanded stent".

24. Close the stopcock so that the fluid path to the catheter is closed and evacuate all air from the inflation/deflation device through the stopcock.

25. Repeat steps 22-24 if necessary, to ensure air contained in the balloon and inflation lumen are removed. Release the inflation/deflation barrel to normal pressure.

Stent deployment

26. Inflate the balloon gradually to expand the stent to the calculated diameter in accordance with the compliance chart. Hold that pressure for 15-30 seconds.

Caution: Inflate to at least the nominal pressure (NP) indicated on the label and the compliance chart. DO NOT exceed Rated Burst Pressure (RBP).

Note: Use multiple fluoroscopy views to verify the stent position and to ensure that the stent has been completely expanded.

27. If necessary, the delivery system balloon may be dilated once more in order to achieve optimum seating of the implanted stent.

28. If the stent is still not completely apposed to the vessel wall, the stent can be re-crossed and further expanded with a larger balloon

Caution: Avoid barotrauma outside the stent margins during post-dilation.

Caution: Exercise care when crossing a newly deployed stent with a coronary guide wire, balloon catheter or stent system to avoid disruption of the stent geometry and stent migration.

Balloon deflation and delivery system removal

29. Deflate the balloon in accordance with standard PCI procedures. Apply negative pressure to the balloon for at least 30 seconds before carefully pulling the delivery system out of the vessel.

30. If the balloon cannot be withdrawn from the stent easily, slightly advance and retract the delivery system very carefully until it is possible to remove.

31. Under fluoroscopic control retrieve the delivery system carefully into the guiding catheter.

Caution: If resistance is encountered at any time during removal of the system follow the instructions for the "Removal of the stent system / delivery system and the guiding catheter as a single unit".

32. Inspect the device immediately upon removal from the patient for any signs of breakage or fragmentation.

33. Observation of the patient and the angiographic evaluation should be performed periodically in the 15 minutes after stent implantation.

Special retrieval techniques

Removal of an unexpanded stent

01. Make sure that the guiding catheter tip and the guide wire are aligned to avoid any acute angle between the guide wire and guiding catheter tip.

02. Slowly pull back the stent system. The entry of the stent into the guiding catheter must be performed slowly under fluoroscopic control to avoid dislodgement of the stent from its position on the delivery system balloon.

Caution: If resistance is encountered at any time during the removal of the system follow the instructions for the "Removal of the stent system / delivery system and the guiding catheter as a single unit".

03. The lesion must be pre-dilated again or otherwise prepared before a second attempt at stenting is undertaken.

Caution: DO NOT RE-INSERT the stent system as the stent and / or the delivery system may have been damaged during the initial attempt to cross the lesion or during withdrawal.

Removal of the stent system / delivery system and the guiding catheter as a single unit

01. Position the proximal balloon marker just distal to the tip of the guiding catheter.

02. Advance the guide wire into the artery as distally as safely possible.

03. Tighten the hemostatic valve secure the delivery system to the guiding catheter.
04. Remove the guiding catheter and the delivery system as a single unit.

Caution: Failure to follow these steps and / or applying excessive force to the stent system can potentially result in loss or damage to the stent and / or delivery system components.

Caution: After use, dispose of the product and packaging in accordance with hospital, administrative and/or local government policy.

Magnetic Resonance Imaging (MRI)

MR conditional

Non-clinical testing has demonstrated that the PRO-Kinetic Energy Cobalt-Chromium Bare Metal Stent is MR Conditional.
A patient with this device can be safely scanned in an MR system meeting the following conditions:

- Static magnetic field of 1.5 T and 3 T
- Maximum spatial field gradient of 3000 gauss/cm (30T/m)
- Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode)

Under the scan conditions defined above, the PRO-Kinetic Energy Cobalt-Chromium Bare Metal Stent is expected to produce a maximum temperature rise of less than 5.7 ºC after 15 minutes of continuous scanning.

In non-clinical testing, the image artifact caused by the device extends approximately 7 mm from the PRO-Kinetic Energy Cobalt-Chromium Bare Metal Stent when imaged with a gradient echo pulse sequence and a 3.0 T MRI system. The artifact may obscure the device lumen.

Summary of Clinical Studies

BIOHELIX-I Clinical Trial

Primary Objective

BIOTRONIK collected clinical data through the BIOHELIX-I clinical trial to establish a reasonable assurance of the safety and effectiveness of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System for the treatment of atherosclerotic disease of native coronary arteries. A summary of the clinical trial is presented below.

Study Design

The BIOHELIX-I study is a prospective, single-arm, multi-center, Investigational Device Exemption (IDE) study designed to evaluate the safety and efficacy of BIOTRONIK's PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System. The PRO-Kinetic Energy Cobalt Chromium (CoCr) Coronary Stent System consists of the PRO-Kinetic Energy Cobalt-Chromium Bare Metal Stent and the associated fast-exchange, balloon-catheter delivery system. In total, the study included 329 evaluable subjects enrolled in 33 study sites located in the United States, Europe and South America.

Patients were considered eligible for the PRO-Kinetic Energy Cobalt-Chromium Bare Metal Coronary Stent implantation if they had a de novo or restenotic lesion in a native coronary artery; restenotic lesions must have been previously treated with only standard PTCA (treatment must be > 12 months prior to the index procedure).Target lesions had to be in a major coronary artery (target vessel). The target vessels included the entire territory of the left anterior descending artery, left circumflex artery or right coronary artery and any major side branch of the artery. A maximum of one target lesion and one non-target lesion could have been treated per subject. The lesions had to be located in separate coronary arteries, with treatment of the non-target lesion occurring first using commercially available therapy (with the exception of brachytherapy). Lesions could have been one solid lesion or a series of multiple, smaller lesions to be treated as one lesion. Target lesions must have been treatable with a single investigational stent; an additional stent may have been used when treating a vessel dissection or another similar intra-procedure complication (use of investigational stent was preferred). Angiographic evidence of ≥ 50% and < 100% stenosis (by operator visual estimate) with a TIMI flow > 1 was required. The target lesion length had to be ≤ 31 mm by operator visual estimate. The target vessel reference diameter had to be 2.25 mm to 4.0 mm by operator visual estimate. Dual antiplatelet therapy was to be administered according to guidelines for one month post-index procedure.

Baseline and post-index procedure angiography for clinical events were analyzed by a central core laboratory. An independent Clinical Events Committee adjudicated major adverse clinical events and stent thrombosis.

The primary endpoint for the BIOHELIX-I study was the target vessel failure (TVF) rate at 9 months post-index procedure. Target vessel failure was defined as cardiac death, myocardial infarction (MI) and ischemia-driven target vessel revascularization (TVR). The TVF rate was compared with a performance goal established from a literature review of recent studies in a similar subject population. The primary endpoint was tested against a performance goal of 18.7%.

The study included several additional secondary endpoints, but no formal hypotheses were associated with the evaluation of the secondary endpoints. Primary and secondary endpoint analyses were conducted on pre-defined analysis populations. Of the 329 patients included in the intent to treat (ITT) analysis population, 320 patients were evaluable for the 9-month primary endpoint.

Clinical follow-up was conducted before discharge and at 1, 9, 12, 24 and 36 months post-index procedure. The study is now considered complete with regard to the 9-month primary endpoint.

Demographics

Baseline characteristics for the BIOHELIX-I Clinical Trial indicated that 68.7% were male, with an average age of 69.0 ± 9.3, 25.5% had diabetes requiring medication, 72.9% had hyperlipidemia requiring medication, 18.2% were current smokers, and 83.6% had hypertension requiring medication.

Baseline Lesion Characteristics

Baseline lesion characteristics included average reference vessel diameter of 2.9 ± 0.5 mm, average minimum lumen diameter of 0.9 ± 0.4 mm, average percent diameter stenosis of 82.9 ± 9.3%, and average lesion length of 13.7 ± 6.0 mm.

Primary Endpoint (9-Month TVF)

The primary endpoint was met. The 9 month TVF rate was 9.06% and the upper 95% confidence bound of 12.76% was less than the pre-specified performance goal of 18.7% ($p < 0.001$). Similar results were found whether the per protocol or the ITT subject populations were analyzed. Table 2 summarizes the TVF rate at 9 months post-index procedure.

Table 2: Primary Endpoint TVF and Components at 9 Months

Intent-to-Treat Analysis (Primary)	9 Months (300 days) Rate (%) [95% CI] n = 320
TVF*	9.06% (29/320) [6.15%, 12.76%]
- Cardiac death	0.95% (3/317) [0.20%, 2.74%]
- MI	1.58% (5/316) [0.52%, 3.65%]
- Ischemia-driven TVR	7.26% (23/317) [4.65%, 10.69%]

*Two patients experienced more than one mechanism of TVF therefore the composite rate of unique subjects is not equivalent to the sum of the components.

Secondary Endpoints

Secondary endpoints were assessed at the specified time points. Key secondary endpoint safety and efficacy results for the ITT population are summarized in Table 3.

Table 3: Key Secondary Endpoint Safety and Effectiveness Results

Secondary Endpoints – ITT Analysis	Rate (%)* [95% CI][1]
TVF at 12 months[2]	11.74% (33/281) [8.22%, 16.10%]
- Cardiac death	1.09% (3/276)
- MI	1.82% (5/275)
- Ischemia-driven TVR	9.75% (27/277)
TVR at 9 months	7.89% (25/317) [5.17%, 11.42%]
- Ischemia-driven TVR	7.26% (23/317)
- Non-ischemia-driven TVR	0.96% (3/314)
TLF at 9 months	8.44% (27/320) [5.63%, 12.04%]
- Cardiac death	0.95% (3/317)
- MI	1.58% (5/316)
- Ischemia-driven TLR	6.62% (21/317)
TLR at 9 months	7.26% (23/317) [4.65%, 10.69%]
- Ischemia-driven TLR	6.62% (21/317)
- Non-ischemia-driven TLR	0.64% (2/314)
All-cause mortality/MI at 9 months	3.13% (10/320) [1.51%, 5.67%]
- All-cause mortality	1.88% (6/319)
- Cardiac	0.95% (3/317)
- Non-cardiac	0.96% (3/313)
- All-cause MI	1.58% (5/316)
Stent thrombosis at 9 months	
Definite	0.94% (3/318)
Probable	0.31% (1/318)
Total Definite/Probable	1.26% (4/318)
Possible	0.94% (3/318)
Stent thrombosis timing – ARC Definite/Probable at 9 months	
Acute (0-24 hours)	0.00% (0/318)
Subacute (>24 hours to 30 days)	0.31% (1/318)
Late (>30 days to 1 year)	0.94% (3/318)
Total Definite/Probable Stent thrombosis	1.26% (4/318)
Acute procedural success	98.8% (325/329)
Device success	99.4% (327/329)
Lesion success	99.4% (327/329)

*Denominators are based on number of subjects with evaluations and/or events occurring within the respective time points.
[1] Confidence Intervals have not been adjusted for multiplicity
[2] The 12-month endpoint results presented in the table are preliminary, due to ongoing data collection and analysis of the time point

Major Clinical Events

The major clinical events that were observed in the ITT population that were serious and adjudicated by the Clinical Events Committee at the time of data analysis are summarized in Table 4. This represents events reported for patients with a mean study follow-up duration of 1.8 ± 0.6 years/ patient.

Table 4: Summary of Major Clinical Events – Study Duration

Category	% (n/329)
Deaths	3.95% (13/329)
Cardiac	1.22% (4/329)
Non-cardiac	2.74% (9/329)
Myocardial infarction events	0.91% (3/329)
Spontaneous MI, Q-wave	0.61% (2/329)
Spontaneous MI, Non Q-wave	0.30% (1/329)
Revascularization events	10.64% (35/329)
TLR	7.90% (26/329)
Ischemia-driven	7.29% (24/329)
Non-ischemia-driven	0.61% (2/329)
Non-TLR TVR	2.74% (9/329)
Ischemia-driven	2.13% (7/329)
Non-ischemia-driven	0.61% (2/329)
Stent thrombosis events, Definite/Probable	1.22% (4/329)
Definite, Subacute	0.30% (1/329)
Definite, Late	0.61% (2/329)
Probable, Late	0.30% (1/329)

Sub-group Analyses

Pre-specified subgroups were examined to determine potential relationships with the primary study endpoint. The TVF rate at 9-months was analyzed in patients with diabetes (12.4%, 11/89), in subjects with small implanted stent diameters (≤ 2.75 mm) (12.1%, 14/116) and in patients > 75 years old (10.0%, 9/90). There were no significant differences in the TVF rate at 9 months for any of the subgroups analyzed.

Summary of Results

The observed rate of target vessel failure at 9 months was 9.06% (29/320, 95% CI: 6.15%, 12.76%) for the ITT population. The observed rate was below the expected rate of 12.7% and met the performance goal of 18.7% ($p < 0.001$). Individual components of the TVF composite rates of cardiac death, myocardial infarction and ischemia-driven TVR at 9 months were low at 0.95%, 1.58% and 7.26%, respectively, in the ITT population. The overall definite/probable rate of stent thrombosis according to ARC definitions was 1.26% (4/318) at 9 months for the ITT population, Acute procedural success was achieved in 98.8% (325/329) of the ITT patients. Device success and lesion success were both achieved in 99.4% (327/329) of the ITT patients. Stable angina was

reduced from 61.4% (202/329) at baseline to 11.0% (34/308) at 9 months post index procedure. The data received and analyzed demonstrate and support the clinical safety and effectiveness of the PRO- Kinetic Energy Cobalt-Chromium Bare Metal Stent in the treatment of atherosclerotic lesion in the coronary arteries.

BIOHELIX-I Study Results by Gender

There was no evidence (p = 1.000) of an association between the primary endpoint and gender. The lack of an observed gender effect for the primary endpoint was also confirmed for analyzed secondary endpoints.

Applicability to Pediatric Population

Coronary artery disease is not typically found in pediatric populations. Accordingly, the safety and effectiveness of the PRO-Kinetic Energy Cobalt Chromium (CoCr) Stent System in pediatric populations were not studied in the BIOHELIX-I trial.

Warranty / Liability

The product and each component of its system (hereinafter "the Product") have been designed, manufactured, tested and packaged with all reasonable care. However, BIOTRONIK has no control over the conditions under which the Product is used and a disturbance of the intended function of the Product may occur for various reasons. In this respect, the warnings in this product publication/instructions for use are expressly to be considered as an integral part of this Disclaimer and provide more detailed information. For this reason, BIOTRONIK disclaims all warranties, expressed or implied regarding the Product, including but not limited to, any warranty of merchantability or fitness for a particular purpose of the Product. Product descriptions or user guidelines in publications do not constitute any expressed representation or any expressed or implied warranty. BIOTRONIK is not liable for any direct, incidental or consequential damages or medical expenses caused by any use, defect, failure or malfunction of the Product whether the claim is based on contract, warranty, tort or otherwise. In transactions related to merchants, damages recoverable from BIOTRONIK will be replacement of the device or direct damages. All consequential damages are excluded. 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 consistent with BIOTRONIK's interest in limiting its liability or warranty without infringing any mandatory provisions of applicable law. No person has any authority to bind BIOTRONIK to any warranty or liability regarding the Product.

Compliance Chart

Table 5: Compliance Chart

Compliance Chart								
Inflation Pressure			Stent Inner Diameter (mm)					
	atm	kPa	2.25	2.5	2.75	3.0	3.5	4.0
NP	9	(912)	2.19	2.42	2.68	3.03	3.56	4.00
	10	(1013)	2.27	2.50	2.77	3.11	3.66	4.14
	11	(1115)	2.35	2.59	2.84	3.18	3.75	4.26
	12	(1216)	2.41	2.66	2.93	3.25	3.83	4.36
	13	(1317)	2.46	2.71	2.99	3.30	3.91	4.45
	14	(1419)	2.51	2.76	3.04	3.35	3.97	4.53
	15	(1520)	2.55	2.80	3.09	3.39	4.02	4.58
RBP	16	(1621)	2.59	2.83	3.13	3.42	4.08	4.63
	17	(1723)	2.63	2.87	3.17	3.45	4.12	4.68
	18	(1824)	2.66	2.90	3.20	3.48	4.15	4.73
NP	In vitro testing has shown that the balloons will reach their nominal size at given NP.							
RBP	In vitro testing has shown that with 95% confidence, 99.9% of the balloons will not burst at or below RBP. DO NOT exceed RBP.							
Note	Diameters at inflation pressures above RBP are provided for information only. At the pressures above RBP shown in this table, 99% of the balloons, with 95% confidence will not burst.							

Symbol Legend

STERILE EO	Sterilized using ethylene oxide		Do not use if package is damaged
	Do not reuse	LOT	Batch code
	Caution, consult accompanying documents	REF	Catalogue number
	Keep dry		Use by
	Keep away from sunlight		Instructions for use
STERILIZE	Do not resterilize	MR	MR conditional
	Date of manufacture		Manufacturer
NP	Nominal Pressure	RBP	Rated Burst Pressure

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