SurVeil™ Drug Coated Balloon

℞ ONLY

Table of Contents

1 DEVICE DESCRIPTION _____ 2
2 INDICATIONS FOR USE _____ 4
3 CONTRAINDICATIONS _____ 4
4 WARNINGS _____ 4
5 PRECAUTIONS _____ 5
6 USE IN SPECIAL POPULATIONS _____ 6
7 DRUG INFORMATION _____ 6
8 POTENTIAL ADVERSE EVENTS _____ 7
9 CLINICAL INFORMATION _____ 7
10 HOW SUPPLIED _____ 33
11 INSTRUCTIONS FOR USE _____ 33
12 DISCLAIMER OF WARRANTY _____ 37

Caution: Federal Law (USA) restricts this device to sale by or on the order of a physician.

1 DEVICE DESCRIPTION

1.1 PTA Catheter Description

The SurVeil™ Drug Coated Balloon Catheter (SurVeil DCB) is a drug transfer balloon designed to restore patency to stenotic peripheral arteries through mechanical dilatation and ancillary delivery of a uniform dose of microcrystalline paclitaxel intended to reduce restenosis. The balloon's excipient polyethyleneimine allows for uniform, targeted transfer and retention of microcrystalline paclitaxel to the vessel wall. Paclitaxel binds to and stabilizes microtubules within cells, arresting the cell division process which prevents cell proliferation.

The SurVeil DCB is a standard 0.035" over-the-wire (OTW) PTA catheter, with a 135 cm usable catheter length and a semi-compliant balloon at the distal tip. As shown in Figure 1, the proximal end is a hub with two female Luer ports, one for the inflation and deflation of the balloon and the other to accommodate a guidewire. The hub connects to a strain relief that minimizes kinking between the stiff hub and the flexible shaft. The shaft tubing size is 5 French and connects the hub to the proximal end of the balloon. The dual lumen shaft tubing is used for inflation/deflation and contains an inner lumen for passage of a guidewire to the distal tip. A portion of the distal catheter shaft is coated with Surmodics™ PhotoLink™ lubricious coating.

The balloon has a cylindrical section, which defines the length of the balloon, with a nominal diameter and a nominal length and a cone section at each end. There are two platinum/iridium radiopaque marker bands placed on the shaft indicating the nominal length of the balloon. The catheter tip, with an atraumatic design, acts as the transition from the catheter to the guidewire.

A compliance chart is included on the product label for each device.

Table 1. Device Characteristics

Balloon Diameter (mm)	Minimum Introducer Sheath	Maximum Crossing Profile (mm)	Nominal Inflation Pressure (atm/bar)	Rated Burst Pressure (atm/bar)
4	5F	1.80 (5.4 Fr)	6	14
5	6F	2.08 (6.2 Fr)	6	14
6	6F	2.15 (6.5 Fr)	6	12
7	7F	2.15 (6.5 Fr)	6	10

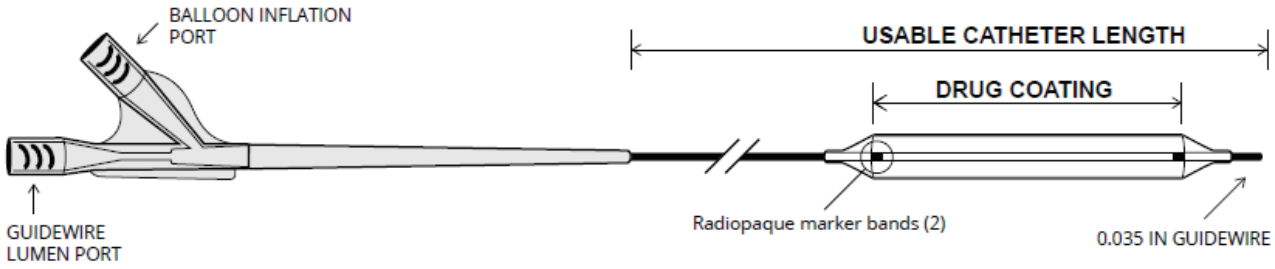
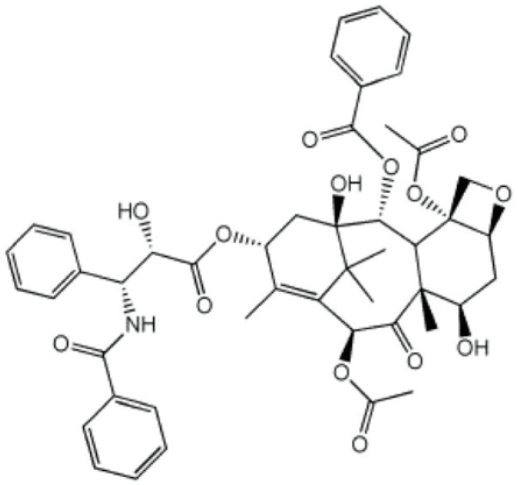


Figure 1. SurVeil™ DCB Catheter

1.2 Drug Coating Description

The drug coating of the SurVeil DCB consists of paclitaxel (active pharmaceutical ingredient) and polyethyleneimine (excipient). The drug coating is uniformly distributed across the balloon surface at a nominal paclitaxel dose density of 2.0 µg/mm² (see nominal paclitaxel dose for each balloon size in Table 2).

Paclitaxel (CAS number 33069-62-4) has the chemical formula $C_{47}H_{51}NO_{14}$ and the following structure:



The polycationic polymer polyethyleneimine (CAS number 9002-98-6) is used as an excipient to facilitate delivery and efficient transfer of the paclitaxel from the balloon to the vessel wall upon balloon expansion. Polyethyleneimine has the following structure:

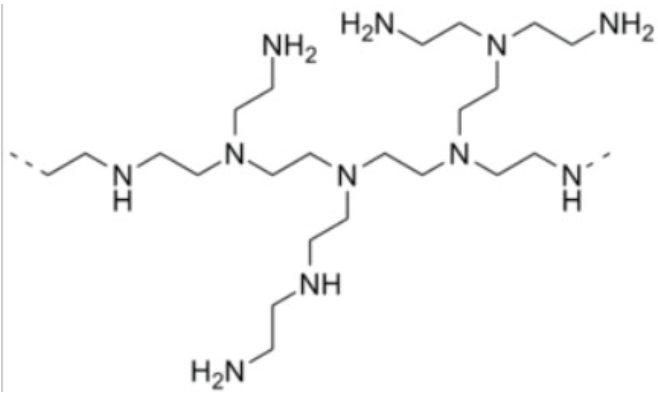


Table 2. Nominal Paclitaxel Dose per Balloon size

Balloon diameter (mm)	Balloon length (mm)					
	40	**60**	**80**	**100**	**120**	**150**
4.0	1005 µg	1508 µg	2011 µg	2513 µg	3016 µg	3770 µg
5.0	1257 µg	1885 µg	2513 µg	3142 µg	3770 µg	4712 µg
6.0	1508 µg	2262 µg	3016 µg	3770 µg	4524 µg	5655 µg
7.0	1759 µg	2639 µg	3519 µg	4398 µg	--	--

2 INDICATIONS FOR USE

The SurVeil DCB is indicated for percutaneous transluminal angioplasty, after appropriate vessel preparation, of *de novo* or restenotic lesions (≤ 180 mm in length) in femoral and popliteal arteries having reference vessel diameters of 4 mm to 7 mm.

3 CONTRAINDICATIONS

The SurVeil DCB is contraindicated for use in:

- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy
- Patients with known hypersensitivity to paclitaxel or structurally related compounds.
- Patients judged to have a lesion that prevents complete inflation of an angioplasty balloon or proper placement of the delivery system.
- Women who are breastfeeding, pregnant or are intending to become pregnant or men intending to father children.
- Coronary, renal and supra-aortic/cerebrovascular arteries.

4 WARNINGS

- **A signal for increased risk of late mortality has been identified following the use of paclitaxel-coated balloons and paclitaxel-eluting stents for femoropopliteal arterial disease beginning approximately 2-3 years post-treatment compared with the use of non-drug coated devices. There is uncertainty regarding the magnitude and mechanism for the increased late mortality risk, including the impact of repeat paclitaxel-coated device exposure. Physicians should discuss this late mortality signal and the benefits and risks of available treatment options with their patients. See CLINICAL INFORMATION section for additional information.**
- **Adhere to the following use parameters for the index procedure:**
  - **Do not use more balloons than necessary. No more than 200 mm of total balloon length should be used, for a total maximum treatable length of 180 mm.**
  - **This product should not be used bilaterally or in multiple lesions that cannot be treated with up to 200 mm total balloon length.**
  - **The safety of exposure to higher doses of the paclitaxel/polyethyleneimine (PEI) drug coating has not been established.**
- The SurVeil DCB is supplied STERILE for SINGLE USE ONLY. Do not reuse and/or resterilize.
- Do not open sterile package until you are ready to begin the procedure.
- Do not use if the integrity of the sterile package has been compromised or if any sterile package or product defects are noted.
- Do not use after the Use by Date on the label.
- Do not exceed the rated burst pressure (RBP) recommended in the compliance chart for this device specified on device packaging.
- To minimize the potential for vessel damage, ensure the expected inflated diameter of the balloon approximates the intended treatment segment.
- Do not use any gaseous medium to inflate the balloon.
- Do not use device if air does not aspirate properly.
- Completely deflate the balloon and maintain negative pressure before withdrawing it from the dilated area.
- The safety and effectiveness of utilizing multiple SurVeil DCBs with a total drug dosage exceeding 9048 µg of paclitaxel in a patient has not been clinically evaluated in the TRANSCEND trial.

DO NOT REUSE and/or RESTERILIZE the SurVeil DCB. Reuse and/or resterilization may create a risk of contamination of the device and/or cause patient infection or cross-infection, including, but not limited to, the transmission of infectious disease(s). Contamination of the device may lead to injury, illness, or death of the patient. Reuse and/or resterilization may compromise integrity of the device, including the drug coating, or lead to device failure, which may result in patient injury, illness, or death. Surmodics is not responsible for any direct, incidental, or consequential damages resulting from reuse and/or resterilization.

5 PRECAUTIONS

- The SurVeil DCB is only to be used by clinicians trained in peripheral vascular percutaneous interventional procedures. A thorough understanding of the technical principles, clinical applications and risks associated with percutaneous transluminal angioplasty is necessary before using the SurVeil DCB.
- Consideration should be given to the risks and benefits of use in patients with a history of non-controllable allergies to contrast solution.
- Use only the recommended balloon inflation solution (50% contrast / 50% sterile saline).
- Administer appropriate drug therapy to the patient according to standard protocols for PTA before insertion of the dilatation catheter
- Take precautions to prevent or reduce clotting when any catheter is used. Flush and rinse all products entering the vascular system with heparinized normal saline or a similar solution. For the SurVeil DCB, flush the guidewire lumen through the guidewire port with heparinized normal saline until the fluid exits the distal tip. Do not rinse or wipe the SurVeil DCB.
- Keep the SurVeil DCB dry prior to insertion into the body. Replace any device that has come into contact with fluids prior to use.
    - Do not immerse the SurVeil DCB in a saline bath.
    - Handle the SurVeil DCB only with dry sterile gloves.
    - Avoid moisture contact with the balloon.
- Minimize contact with the coated balloon. Extended manipulation of the SurVeil DCB can cause loss of coating integrity.
- Keep the balloon sheath in place during preparation of the SurVeil DCB. Remove the balloon sheath immediately before placing over guidewire.
- If difficulty is encountered while removing the balloon sheath, discard device and use a new SurVeil DCB.
- Do not attempt to pass the SurVeil DCB through an introducer that is smaller than indicated in the list of required materials or on the primary package label.
- Do not inflate the balloon outside the body or prior to reaching the target segment as it may disrupt the drug coating.
- Always advance and withdraw the SurVeil DCB under negative pressure.
- Do not use the SurVeil DCB if the shaft has been bent or kinked because device function could be compromised.
- Do not advance the SurVeil DCB if resistance is met.
- Do not move the guidewire or reposition once inflation has begun.
- Only change the position of the balloon catheter with the guidewire in place.
- Do not over-tighten the hemostatic valve around the SurVeil DCB as lumen constriction may occur, affecting inflation/deflation of the balloon. Advance the SurVeil DCB to the target segment in an efficient manner and immediately inflate.
- To prevent over-pressurization, use a pressure monitoring device.

- Minimize the number of contrast solution injections during positioning to ensure appropriate drug delivery to lesion.
- Use of the SurVeil DCB in conjunction with other drug-eluting stents or drug-coated balloons in the same procedure or following treatment failure has not been evaluated.

Pre- and post-procedure medication regimen
It is strongly advised that the treating physician follow the Inter- Society Consensus (TASC II) Guidelines recommendations (or other applicable country guidelines) for antiplatelet therapy pre- and post-procedure.

6 USE IN SPECIAL POPULATIONS

- Pediatric Use: The safety and effectiveness of the SurVeil DCB has not been established in pediatric patients (<21 years of age).
- Pregnancy and Lactation: The SurVeil DCB has not been studied in women who are breastfeeding, pregnant, or are intending to become pregnant, or men intending to father children.

7 DRUG INFORMATION

7.1 Mechanism of Action

The SurVeil DCB coating contains paclitaxel, a pharmaceutical agent that inhibits the proliferation of smooth muscle cells and fibroblasts in the intimal and medial layers of the vessel. Paclitaxel binds to and stabilizes microtubules within the cells, which arrests the cell division process.

7.2 Drug Interactions

Formal drug interaction studies have not been conducted for SurVeil DCB. The respective instructions for use for all drugs used in conjunction with SurVeil DCB should be consulted for interactions with paclitaxel. Consideration should be given to the potential for systematic and local drug interactions in the vessel wall in a patient who is taking a drug with known interactions with paclitaxel or when deciding to initiate drug therapy in a patient who has been treated with the SurVeil DCB.

7.3 Carcinogenicity, Genotoxicity, and Reproductive Toxicology

No long-term studies in animals have been published in peer-reviewed literature to evaluate the carcinogenic potential of paclitaxel. Paclitaxel was not mutagenic in the Ames test or the CHO/HGPRT gene mutation assay. However, the mechanism by which paclitaxel interferes with cellular proliferation may give rise to loss of chromosomes during cell division as a result of microtubule stabilization during cell division. It has not been established that paclitaxel exerts any direct action on DNA to induce strand fragmentation.

Reproductive toxicity has been previously evaluated in vivo in both rabbits and rats. When administered during rabbit fetal organogenesis, paclitaxel doses of 3.0 mg/kg/day caused embryo- and fetotoxicity; maternal toxicity was also observed. No teratogenic effects were observed at 1.0 mg/kg/day; effects at higher doses could not be assessed due to fetal mortality. In rats, fertility impairment was observed at doses ≥ 1 mg/kg/day.

For comparison, the worst-case dose of paclitaxel delivered by the SurVeil DCB (assuming maximum size and number of balloons used in a lesion) is 9048 µg, which is approximately 6 and 19 times less than the dose that saw effects in rats and rabbits, respectively, when normalized to body weight.

8 POTENTIAL ADVERSE EVENTS

Potential adverse events, which may be associated with the use of a peripheral-dilatation balloon catheter procedure may include, but are not limited to, the following:

- Acute re-occlusion necessitating surgical intervention
- Allergic reaction to contrast solution, anti-platelet therapy, or catheter system components
- Amputation
- Aneurysm
- Arrhythmias
- Arterio-venous fistula
- Bleeding
- Death
- Endocarditis
- Femoral nerve compression with associated neuropathy
- Groin area bruising and discomfort
- Ischemia or infarction of tissue/organ
- Renal insufficiency or failure
- Local hematoma
- Local hemorrhage
- Local infections
- Local or distal thromboembolic episodes
- Low blood pressure
- Pain and tenderness
- Pseudoaneurysm
- Pyrogenic reaction
- Respiratory failure
- Restenosis of the dilated artery
- Sepsis/infection
- Short-term hemodynamic deterioration
- Stroke
- Systemic embolization
- Total occlusion or thrombosis
- Vessel damage, dissection, perforation, rupture, or spasm

Potential adverse events that may be unique to the paclitaxel drug coating may include, but are not limited to:

- Allergic/immunologic reaction
- Alopecia
- Anemia
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage, or necrosis
- Myalgia/arthralgia
- Myelosuppression
- Peripheral neuropathy

9 CLINICAL INFORMATION

9.1 Late Mortality Signal for Paclitaxel-Coated Devices

A meta-analysis of 28 randomized controlled trials published in December 2018 by Katsanos et. al. identified an increased risk of late mortality at 2 years and beyond for paclitaxel-coated balloons and paclitaxel-eluting stents used to treat femoropopliteal arterial disease. In response to these data, FDA performed a patient-level meta-analysis of long-term follow-up data from the pivotal premarket randomized trials of paclitaxel-coated devices used to treat femoropopliteal disease using available clinical data through May 2019. The meta-analysis also showed a late mortality signal in study subjects treated with paclitaxel-coated devices compared to patients treated with uncoated devices. Specifically, in the 3 randomized trials with a total of 1090 patients and available 5-year data, the crude mortality rate was 19.8% (range 15.9% - 23.4%) in patients treated with paclitaxel-coated devices compared to 12.7% (range 11.2% - 14.0%) in subjects treated with uncoated devices. The relative risk for increased mortality at 5 years was 1.57 (95% confidence interval 1.16 - 2.13), which corresponds to a 57% relative increase in mortality in patients treated with paclitaxel-coated devices. An independent meta-analysis of similar patient-level data provided by VIVA Physicians, a vascular medicine organization, reported similar findings with a hazard ratio of 1.38 (95% confidence interval 1.06 - 1.80).

The presence and magnitude of the late mortality risk should be interpreted with caution because of multiple limitations in the available data, including wide confidence intervals due to a small sample size, pooling of studies of different paclitaxel-coated devices that were not intended to be combined, substantial amounts of missing study data, no clear evidence of a paclitaxel dose effect on mortality, and no identified pathophysiologic mechanism for the late deaths. Paclitaxel-coated balloons and stents improve blood flow to the legs and decrease the likelihood of repeat procedures to reopen blocked blood vessels compared to uncoated devices. The benefits of paclitaxel-coated devices (e.g., reduced reinterventions) should be considered in individual patients along with potential risks (e.g., late mortality).

In the TRANSCEND Trial, follow-up has completed through one year and follow-up through five years is ongoing. In the TRANSCEND Trial, the Kaplan Meier mortality estimates at 12 months, 24 months, and 36 months are represented in Table 3 below. Additional information regarding outcomes can be found in section 9.3.

Table 3. Mortality Estimate - TRANSCEND

Mortality	SurVeil DCB (N=222 subjects)	IN.PACT Admiral DCB (N=224 subjects)
12 months	7 (3.33%)	7 (3.17%)
24 months	17 (8.36%)	16 (7.29%)
36 months	22 (10.99%)	26 (12.07%)

Number of events and Kaplan-Meier cumulative incidence rate

9.2 TRANSCEND Trial

The clinical evidence supporting the safety and effectiveness of the SurVeil™ Drug-Coated Balloon for the treatment of *de novo* or restenotic lesions ≤180 mm in length in femoral and popliteal arteries having reference vessel diameters (RVD) of 4 mm to 7 mm is from the TRANSCEND study.

A study titled “The Randomized And Controlled Noninferiority Trial to Evaluate Safety and Clinical Efficacy of the SurVeil™ Drug-Coated Balloon iN the Treatment of Subjects with Stenotic Lesions of the Femoropopliteal Artery Compared to the Medtronic IN.PACT® Admiral® Drug-Coated Balloon” (TRANSCEND) was conducted. The TRANSCEND Study is a global, prospective, multi-center, single-blind, 1:1 randomized (SurVeil DCB vs IN.PACT Admiral DCB), controlled non-inferiority trial.

9.2.1 Primary Objective

The primary objective of the study was to determine whether the SurVeil™ Drug-Coated Balloon Catheter showed acceptable performance in long-term (12-month) safety rates and vessel patency when treating femoropopliteal lesions.

9.2.2 Study Design

A total of 446 subjects were randomized in the TRANSCEND study. Subjects were randomized at 65 centers located in the United States, Australia, New Zealand, and Europe. Subject follow up is ongoing and will extend for 5 years post index procedure.

Eligible subjects were 18 years or older and consented to participate in the study. These subjects had documented peripheral artery disease defined as Rutherford categories 2, 3, or 4 and evidence of a stenotic, restenotic or occlusive lesion(s) located ≥10 mm below the common femoral bifurcation and terminated distally at or above the end of the P1 segment of the popliteal artery with a degree of stenosis ≥70% by angiographic visual estimate. The vessel diameter was between ≥4 mm and ≤7 mm and a total lesion length (one long lesion or multiple serial lesions) of ≤180 mm. Subject follow up is occurring at 1 month, 6 months, 12 months, 2 years, 3 years, 4 years and 5 years after the index procedure.

Data collected through November 13, 2020 on the full TRANSCEND study cohort is included below.

The primary study endpoints were as follows:

- Primary Safety Endpoint
  - The primary safety endpoint was a composite of freedom from device- and procedure-related death through 30 days post-index procedure and freedom from major target limb amputation (above the ankle) and clinically-driven target vessel revascularization (TVR) through 12 months post-index procedure. This effectiveness endpoint was designed to demonstrate that the 12 month safety for the SurVeil™ Drug-Coated Balloon is non-inferior to the Medtronic IN.PACT® Admiral® Drug-Coated Balloon.
- Primary Effectiveness Endpoint
  - The primary effectiveness endpoint was primary patency, defined as a composite of freedom from clinically-driven TLR and binary restenosis (restenosis defined as DUS peak systolic velocity ratio [PSVR] ≥2.4 or ≥50% stenosis as assessed by independent angiographic and DUS core labs) through 12 months post-index procedure. This effectiveness endpoint was designed to demonstrate that the 12 month primary patency for the SurVeil™ Drug-Coated Balloon is non-inferior to the Medtronic IN.PACT® Admiral® Drug-Coated Balloon.

The secondary study endpoints were as follows:

- Device Success: defined as successful delivery, balloon inflation, deflation and retrieval of the intact study device without burst below rated burst pressure, and achievement of <50% residual stenosis of the target lesion (by core lab-assessed quantitative angiography [QA]) without flow-limiting arterial dissection using only the study device
- Technical Success: defined as achievement of a final residual diameter stenosis of <50% (by core lab-assessed QA) without flow-limiting arterial dissection at the end of the procedure
- Procedure Success: defined as evidence of both acute technical success and absence of Peripheral Academic Research Consortium major adverse events (PARC MAEs; e.g., death, stroke, myocardial infarction, acute onset of limb ischemia, index bypass graft or treated segment thrombosis, and or need for urgent/emergent vascular surgery) within 72 hours of the index procedure
- Freedom from all-cause death, major target limb amputation and TVR through 30 days
- Primary patency through 24 months
- Target vessel patency, defined as freedom from clinically-driven TVR and binary restenosis restenosis defined as DUS PSVR ≥2.4 or ≥50% stenosis as assessed by independent angiographic and DUS core labs), within 12 and 24 months

- Sustained clinical improvement, defined as freedom from major target limb amputation, TVR and worsening target limb Rutherford class, within 6, 12, and 24 months
- Clinically-driven TLR, within 6, 12, 24, 36, 48, and 60 months
- Historical major adverse events (Historical MAEs), defined as composite of all-cause death, clinically-driven TLR, major target limb amputation, or thrombosis at the target lesion, within 6, 12, 24, 36, 48, and 60 months
- Major target-limb amputation, within 6, 12, 24, 36, 48, and 60 months
- Thrombosis at the target lesion, within 6, 12, 24, 36, 48, and 60 months
- Change in target limb Rutherford class from baseline to 1, 6, 12, and 24 months
- Change in target limb PARC class from baseline to 1, 6, 12, and 24 months
- Decrease in target limb resting ankle brachial index ABI) or toe brachial index TBI) ≥0.15 from baseline to 6, 12, and 24 months
- Change in Walking Impairment Questionnaire (WIQ) score from baseline to 1, 12, and 24 months
- Change in 6-minute walk test (6-MWT) from baseline to 12 and 24 months
- Change in Peripheral Artery Questionnaire (PAQ) score from baseline to 1, 12, and 24 months

The TRANSCEND study utilized independent duplex ultrasound and angiographic core labs to review and analyze key study variables. Adjudication of any potential major adverse events and endpoint events for the study was conducted by an independent Clinical Events Committee (CEC). Trial performance and safety of enrolled patients was monitored by an independent Data Monitoring Committee.

9.2.3 Patient Population

Table 4 provides a review of baseline demographics and medical history of the 446 subjects enrolled into the TRANSCEND study.

Table 4. Baseline Demographics and Medical History – TRANSCEND RCT (N=446)

Patient Characteristics	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Demographics		
Age (years)		
Mean ± SD (N)	68.7±9.4 (222)	67.4±9.3 (224)
Median (Q1,Q3)	69.0 (62.0,76.0)	67.0 (60.0,74.0)
Range (Min,Max)	(44.0,93.0)	(38.0,99.0)
Male	62.6% (139/222)	63.4% (142/224)
Race		
White	86.0% (191/222)	88.8% (199/224)
Black or African American	10.4% (23/222)	9.4% (21/224)
Asian	0.5% (1/222)	0.4% (1/224)
Native Hawaiian or Other Pacific Islander	0.0% (0/222)	0.0% (0/224)
American Indian or Alaska Native	0.5% (1/222)	0.0% (0/224)
Other	0.5% (1/222)	0.9% (2/224)
Not Answered	2.3% (5/222)	0.4% (1/224)
Ethnicity		
Hispanic or Latino	2.7% (6/222)	3.1% (7/224)
Not Hispanic or Latino	95.5% (212/222)	96.4% (216/224)
Not Answered	1.8% (4/222)	0.4% (1/224)
Medical History		

Patient Characteristics	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Smoking Status		
Current Smoker	41.9% (93/222)	37.9% (85/224)
Former Smoker	42.8% (95/222)	46.0% (103/224)
Never Smoked	15.3% (34/222)	16.1% (36/224)
Diabetes Mellitus	41.4% (92/222)	40.2% (90/224)
Diabetes Control Method		
No Treatment	1.1% (1/92)	1.1% (1/90)
Diet and/or Exercise Only	7.6% (7/92)	2.2% (2/90)
Oral or Other Non-Insulin Therapies	51.1% (47/92)	58.9% (53/90)
Requiring Insulin	40.2% (37/92)	37.8% (34/90)
Rutherford Classification at Baseline		
2 - Moderate claudication	21.6% (48/222)	34.4% (77/224)
3 - Severe claudication	75.7% (168/222)	61.2% (137/224)
4 - Ischemic rest pain	2.7% (6/222)	4.5% (10/224)
Hypertension	91.4% (203/222)	87.9% (197/224)
Hypercholesterolemia	86.5% (192/222)	86.6% (194/224)
Chronic Angina	6.8% (15/221)	7.2% (16/223)
Ischemic Heart Disease	27.1% (59/218)	28.6% (64/224)
Myocardial Infarction	22.4% (49/219)	21.0% (46/219)
PCI	34.8% (77/221)	32.9% (73/222)
CABG	19.8% (44/222)	21.5% (48/223)
TIA	4.5% (10/221)	5.4% (12/221)
CVA	6.8% (15/221)	10.8% (24/223)
CVA Type		
Ischemic	33.3% (5/15)	41.7% (10/24)
Hemorrhagic	0.0% (0/15)	8.3% (2/24)
Unknown	66.7% (10/15)	50.0% (12/24)
CHF	10.4% (23/221)	9.0% (20/222)
Chronic Renal Insufficiency	22.5% (50/222)	10.8% (24/223)
Renal Failure	2.7% (6/221)	0.4% (1/224)
Previous Lower Extremity Artery Revascularization	31.5% (70/222)	36.8% (82/223)
History of Deep Venous Thromboembolism	4.1% (9/220)	3.6% (8/224)
Thromboembolism Type		
Deep Venous Thromboembolism	100.0% (9/9)	75.0% (6/8)
Pulmonary Embolism	0.0% (0/9)	12.5% (1/8)
Unknown	0.0% (0/9)	12.5% (1/8)
History of Lower Limb Amputation	0.5% (1/222)	0.0% (0/224)
Family History of PAD	7.6% (13/170)	11.1% (18/162)
Family History of CAD	47.0% (87/185)	50.3% (89/177)

9.2.4 Lesion Characteristics

Table 5 presents the baseline lesion characteristics, procedural characteristics, and post procedure measurements for the TRANSCEND study.

Table 5. Angiographic Core Lab Baseline, Procedural, Post-procedure Reported Lesion Characteristics

Characteristics	SurVeil DCB (N=222 Subjects L=222 Lesions)	IN.PACT Admiral DCB (N=224 Subjects L=224 Lesions)
Pre-Procedure Morphology		
Vessel Location		
SFA		
Proximal	11.8% (26/221)	9.9% (22/223)
Mid	40.3% (89/221)	40.4% (90/223)
Distal	42.5% (94/221)	41.3% (92/223)
Ostial	0.0% (0/221)	1.8% (4/223)
Popliteal		
Proximal	3.6% (8/221)	5.4% (12/223)
Mid	1.8% (4/221)	0.9% (2/223)
Distal	0.0% (0/221)	0.4% (1/223)
Lesion Length (mm)		
Mean ± SD (N)	72.5±48.4 (221)	70.0±50.5 (223)
Median (Q1,Q3)	60.6 (33.1,99.0)	55.7 (28.2,99.0)
Range (Min,Max)	(10.5,215.0)	(9.8,232.8)
Eccentric	21.7% (48/221)	25.1% (56/223)
Bend		
<45 degrees	100.0% (221/221)	100.0% (223/223)
≥45 degrees to <90 degrees	0.0% (0/221)	0.0% (0/223)
≥90 degrees	0.0% (0/221)	0.0% (0/223)
Thrombus	0.0% (0/221)	0.4% (1/223)[1]
Calcification		
None/Mild	50.7% (112/221)	48.0% (107/223)
Moderate	36.2% (80/221)	41.3% (92/223)
Severe	13.1% (29/221)	10.8% (24/223)
Ulcerated	7.7% (17/221)	5.4% (12/223)
Aneurysm	0.0% (0/221)	0.0% (0/223)
Ectasia	5.0% (11/221)	4.5% (10/223)
Blood Flow		
Normal	73.8% (163/221)	72.2% (161/223)
Decreased	3.6% (8/221)	2.7% (6/223)
No Flow	22.6% (50/221)	25.1% (56/223)
Collaterals	24.0% (53/221)	27.8% (62/223)
Collateral Grade		
1-Minimal	1.9% (1/53)	1.6% (1/62)
2-Moderate	22.6% (12/53)	33.9% (21/62)
3-Good	75.5% (40/53)	64.5% (40/62)
Occluded[2]	22.2% (49/221)	26.5% (59/223)

Characteristics	SurVeil DCB (N=222 Subjects L=222 Lesions)	IN.PACT Admiral DCB (N=224 Subjects L=224 Lesions)
Pre-Procedure Quantitative Vascular Angiography		
RVD (mm)[3]		
Mean ± SD (N)	5.3±0.9 (221)	5.3±0.7 (223)
Median (Q1,Q3)	5.2 (4.6,5.8)	5.2 (4.7,5.8)
Range (Min,Max)	(3.2,8.4)	(3.7,8.4)
MLD (mm)[4]		
Mean ± SD (N)	1.4±1.1 (221)	1.3±1.0 (223)
Median (Q1,Q3)	1.5 (0.5,2.2)	1.3 (0.0,2.0)
Range (Min,Max)	(0.0,4.4)	(0.0,4.3)
Diameter Stenosis (%)[5]		
Mean ± SD (N)	72.9±18.8 (221)	75.8±18.1 (223)
Median (Q1,Q3)	71.1 (58.0,87.5)	74.4 (60.5,100.0)
Range (Min,Max)	(22.0,100.0)	(31.2,100.0)
Post-Procedure		
Thrombus	0.0% (0/217)	0.0% (0/223)
Spasm	0.0% (0/217)	0.0% (0/223)
Abrupt Closure	0.0% (0/217)	0.0% (0/223)
No Reflow	0.0% (0/217)	0.0% (0/223)
Distal Embolization	0.0% (0/217)	0.0% (0/222)
Perforation		
0	100.0% (217/217)	100.0% (223/223)
I	0.0% (0/217)	0.0% (0/223)
II	0.0% (0/217)	0.0% (0/223)
III	0.0% (0/217)	0.0% (0/223)
Blood Flow		
Normal	100.0% (217/217)	100.0% (223/223)
Decreased	0.0% (0/217)	0.0% (0/223)
No Flow	0.0% (0/217)	0.0% (0/223)
Dissection		
None	41.9% (91/217)	48.0% (107/223)
A	11.5% (25/217)	11.2% (25/223)
B	24.9% (54/217)	25.1% (56/223)
C	17.1% (37/217)	11.2% (25/223)
D	4.6% (10/217)	4.5% (10/223)
E	0.0% (0/217)	0.0% (0/223)
F	0.0% (0/217)	0.0% (0/223)
Staining	0.0% (0/215)	0.0% (0/222)
Quantitative Vascular Angiography		
RVD (mm)[1]		
Mean ± SD (N)	5.3±0.9 (217)	5.3±0.8 (223)
Median (Q1,Q3)	5.3 (4.7,5.9)	5.3 (4.8,5.8)
Range (Min,Max)	(3.4,8.4)	(3.7,8.4)
MLD (mm)[2]		
Mean ± SD (N)	4.3±0.8 (217)	4.3±0.7 (223)
Median (Q1,Q3)	4.3 (3.9,4.8)	4.2 (3.8,4.8)
Range (Min,Max)	(2.5,6.6)	(2.6,6.9)
Diameter Stenosis (%)[3]		
Mean ± SD (N)	18.7±9.6 (217)	18.9±9.3 (223)

Characteristics	SurVeil DCB (N=222 Subjects L=222 Lesions)	IN.PACT Admiral DCB (N=224 Subjects L=224 Lesions)
Median (Q1,Q3) Range (Min,Max)	17.9 (11.4,25.6) (-1.6,45.0)	18.8 (13.1,24.7) (-3.5,47.1)
Procedural Characteristics		
Pre-dilatation Performed	100.0% (222/222)	100.0% (224/224)
Post-dilatation Performed	18.0% (40/222) [6]	17.4% (39/224)
Bailout Stenting Performed	8.1% (18/222)	6.7% (15/224)
Device Success[7]	92.1% (199/216)	93.7% (208/222)
Technical Success[8]	100.0% (217/217)	100.0% (223/223)
Procedure Success[9]	99.5% (217/218)	99.6% (222/223)

[1] Per the angiographic core laboratory, subject 115-009 had thrombus in the target vessel.

[2] Occluded was defined as 100% diameter stenosis.

[3] RVD was calculated as the average of the distal and proximal user-defined target lesion normal references from 2 projections.

[4] MLD is based on the average of 2 projections.

[5] Percent diameter stenosis was calculated as follows: 1−minimum lumen diameter/RVD ×100.

[6] SurVeil DCB subject 117-019 had post-dilatation performed using 2 post dilatation balloons.

[7] Device Success: defined as successful delivery, balloon inflation, deflation and retrieval of the intact study device without burst below rated burst pressure, and achievement of <50% residual stenosis of the target lesion (by core lab-assessed QA) without flow-limiting arterial dissection, using only the study device.

[8] Technical Success: defined as achievement of a final residual diameter stenosis of <50% without flow-limiting arterial dissection at the end of the procedure.

[9] Procedure Success: defined as evidence of both acute technical success and absence of PARC MAEs (e.g., death, stroke, myocardial infarction, acute onset of limb ischemia, index bypass graft or treated segment thrombosis, and or need for urgent/ emergent vascular surgery) within 72 hours of the index procedure.

9.2.5 Results

9.2.5.1 Primary Safety Endpoint Results

Table 6 presents the primary safety results for the full study cohort. The SurVeil™ Drug-Coated Balloon will be concluded to be non-inferior to the IN.PACT® Admiral® Drug-Coated Balloon for the primary safety endpoint if the one-sided lower 97.5% confidence bound on the difference between groups (SurVeil DCB vs. IN.PACT DCB) is less than 10% (non-inferiority margin). In the ITT group, using multiple imputation, the rate of the primary safety endpoint was 91.7% in the Surveil DCB group compared to 89.6% in the IN.PACT Admiral DCB group. The difference in rates between the groups was 2.1% with one-sided lower 97.5% CL of -4.0%. Since this is higher than the pre-specified non-inferiority margin of -10.0%, non-inferiority is met (P-value for non-inferiority <0.0001) and the SurVeil DCB is declared non-inferior to the IN.PACT Admiral DCB with regards to the primary safety endpoint. A complete case analysis was carried out as a sensitivity analysis on ITT subjects with available data (i.e., subjects who experienced the primary safety composite or had at least 335 days of follow-up) and provided similar results. Kaplan-Meier plot of primary safety through 395 days is presented in Figure 2.

Table 6. Primary Safety – Full Cohort, Intent-to-Treat (N=446)

Primary Safety Endpoint	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)	Difference [One-sided Lower 97.5% CL]	Non-inferiority Test P-value[1]
Composite of freedom from device- and procedure-related death through 30 days and freedom from major target limb amputation and clinically-driven TVR through 12 months (ITT – Multiple Imputations)	**91.7% (87.9%,95.5%)**	**89.6% (85.5%,93.7%)**	**2.1% [-4.0%]**	**<0.0001**
Composite of freedom from device- and procedure-related death through 30 days and freedom from major target limb amputation and clinically-driven TVR through 12 months (ITT - Complete Case)	92.0% (183/199)	89.9% (195/217)	2.1% [-4.0%]	<0.0001
Freedom from device- and procedure-related death through 30 days[2]	99.5% (217/218)	100.0% (223/223)		
Freedom from clinically-driven TVR through 12 months[3]	92.4% (183/198)	89.9% (195/217)		
Freedom from major target limb amputation through 12 months[4]	100.0% (196/196)	100.0% (215/215)		

[1] P-value is derived from one-sided Farrington-Manning test with noninferiority margin of 10% and a one-sided significance level of 0.025.

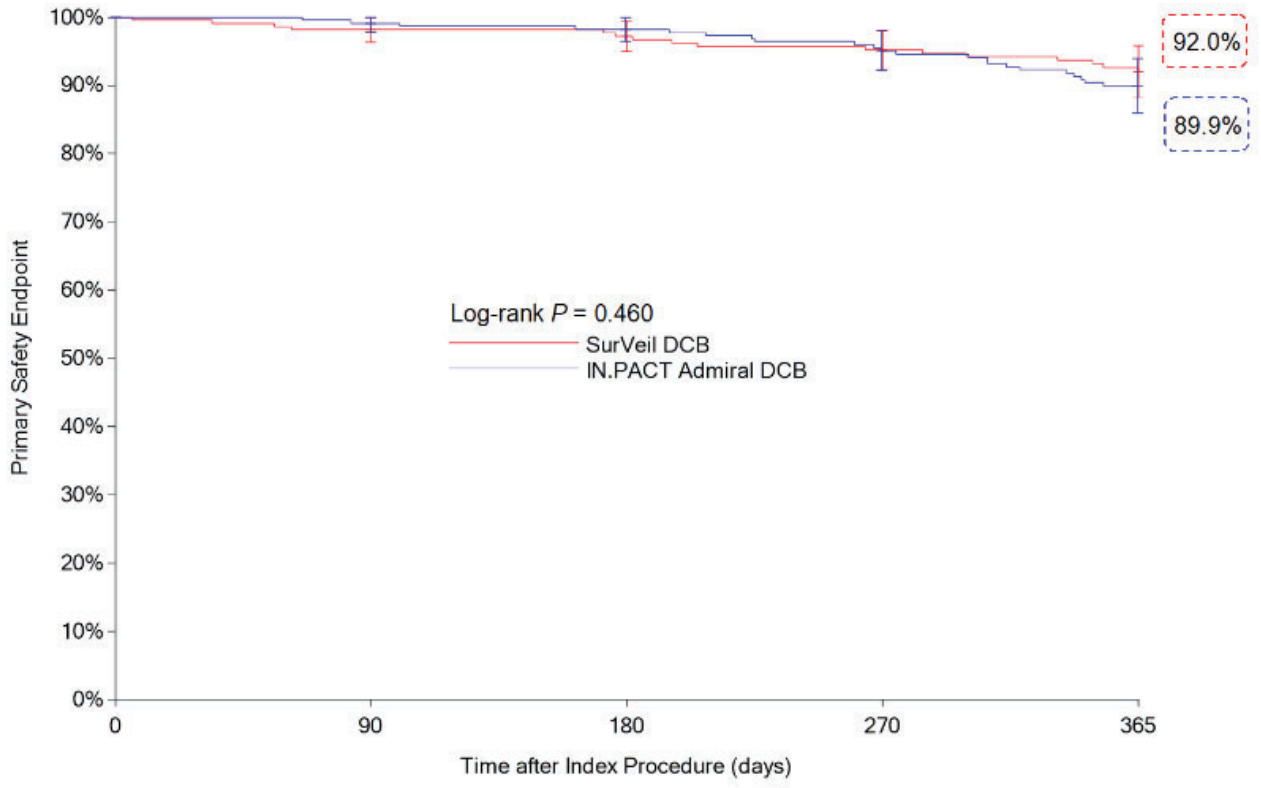
[2] Denominators include subjects with at least 28 days of follow-up or subjects experiencing device- or procedure-related death through 30 days.

[3] Denominators include subjects with at least 335 days of follow-up or subjects experiencing clinically-driven TVR through 365 days.

[4] Denominators include subjects with at least 335 days of follow-up or subjects experiencing target limb amputation through 365 days.

Primary Safety Endpoint		0	[1, 90]	[91, 180]	[181, 270]	[271, 365]
SurVeil DCB (N=222 Subjects)	# Entered	222	222	209	202	193
	# Censored	0	9	5	5	53
	# Events	0	4	2	4	6
	Event-free [%]	100.0%	98.1%	97.2%	95.2%	92.0%
	Greenwood SE [%]	0.0%	0.9%	1.1%	1.5%	1.9%
IN.PACT Admiral DCB (N=224 Subjects)	# Entered	224	223	220	217	209
	# Censored	1	1	1	1	48
	# Events	0	2	2	7	11
	Event-free [%]	100.0%	99.1%	98.2%	95.0%	89.9%
	Greenwood SE [%]	0.0%	0.6%	0.9%	1.5%	2.0%
Tests Between Groups		Test	Chi-Square	Degree of Freedom	P-value	
		Log-Rank	0.5455	1	0.460	

Note: The p-value should be interpreted with caution because a hypothesis test for the survival endpoint was not pre-specified and was not adjusted for multiplicity



Number at risk					
SurVeil DCB	222	209	202	193	139
IN.PACT Admiral DCB	224	220	217	209	154

Figure 2. Kaplan-Meier Curve for the Primary Safety Endpoint to 12 Months - ITT Analysis Population (N=446)

9.2.5.2 Primary Efficacy Endpoint Results

Table 7 presents the primary efficacy results for the full study cohort. The SurVeil™ Drug-Coated Balloon will be concluded to be non-inferior to the IN.PACT® Admiral® Drug-Coated Balloon for the primary efficacy endpoint of primary patency if the one-sided lower 97.5% confidence bound on the difference between groups (SurVeil DCB vs. IN.PACT DCB) is less than 15% (non-inferiority margin). In the ITT group, using multiple imputation, the rate of primary patency at 12 months was 81.7% in the Surveil DCB group compared to 85.9% in the IN.PACT Admiral DCB group. The difference in rates between the groups was -4.2% with one-sided lower 97.5% CL of -12.0%. Since this is higher than the pre-specified noninferiority margin of -15.0%, non-inferiority is met (P-value for non-inferiority 0.0035) and the SurVeil DCB is declared non-inferior to IN.PACT Admiral DCB with respect to the primary efficacy endpoint. A complete case analysis was carried out on ITT subjects with available data (i.e., subjects who experienced the primary effectiveness composite or had at least 335 days of follow-up) and provided similar results. Kaplan-Meier plot of primary patency through 12 months is presented in Figure 3.

Table 7. Primary Efficacy – Full Cohort, Intent-to-Treat (N=446)

Primary Effectiveness Endpoint	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)	Difference [One-sided Lower 97.5% CL]	Non-inferiority Test P-value[1]
Primary patency through 12 months (ITT – Multiple Imputation)	**81.7% (75.9%,87.4%)**	**85.9% (80.9%,90.9%)**	**-4.2% [-12.0%]**	**0.0035**
Primary patency through 12 months (ITT - Complete Case)	82.2% (139/169)	86.7% (163/188)	-4.5% [-12.3%]	0.0041
Freedom from clinically driven TLR through 12 months[2]	91.9% (182/198)	94.4% (203/215)		
Freedom from binary restenosis through 12 months[3]	88.0% (139/158)	91.2% (165/181)		

[1] P-value is derived from one-sided Farrington-Manning test with noninferiority margin of 15% and a one-sided significance level of 0.025.

[2] Denominators include subjects with at least 335 days of follow-up or subjects experiencing clinically-driven TLR through 395 days.

[3] Denominators include subjects with evaluable 12-month DUS (within or outside the visit window of 365±30 days) or subjects whose stenosis status could have been imputed from later assessments.

Primary Patency Failure	0	[1, 90]	[91, 180]	[181, 270]	[271, 365]	[366-395]
SurVeil DCB (N=222 Subjects) # Entered	222	222	211	204	195	128
# Censored	0	10	5	5	52	31
# Events	0	1	2	4	15	8
Event-free [%]	100.0%	99.5%	98.6%	96.6%	88.0%	81.7%
Greenwood SE [%]	0.0%	0.5%	0.8%	1.3%	2.4%	3.1%
IN.PACT Admiral DCB (N=224 Subjects) # Entered	224	223	221	218	214	152
# Censored	1	1	1	2	47	30
# Events	0	1	2	2	15	5
Event-free [%]	100.0%	99.6%	98.7%	97.7%	90.3%	86.9%
Greenwood SE [%]	0.0%	0.4%	0.8%	1.0%	2.1%	2.5%
Tests Between Groups	Test	Chi-Square	Degree of Freedom	P-value		
	Log-Rank	1.4592	1	0.227		

The time to primary patency failure was defined as the time to binary restenosis based on date of 12-month DUS or clinically-driven TLR event date, whichever was earlier. For those who did not have primary patency failure, follow-up days were used.

Note: the p-value should be interpreted with caution because a hypothesis test for the survival endpoint was not pre-specified and was not adjusted for multiplicity.

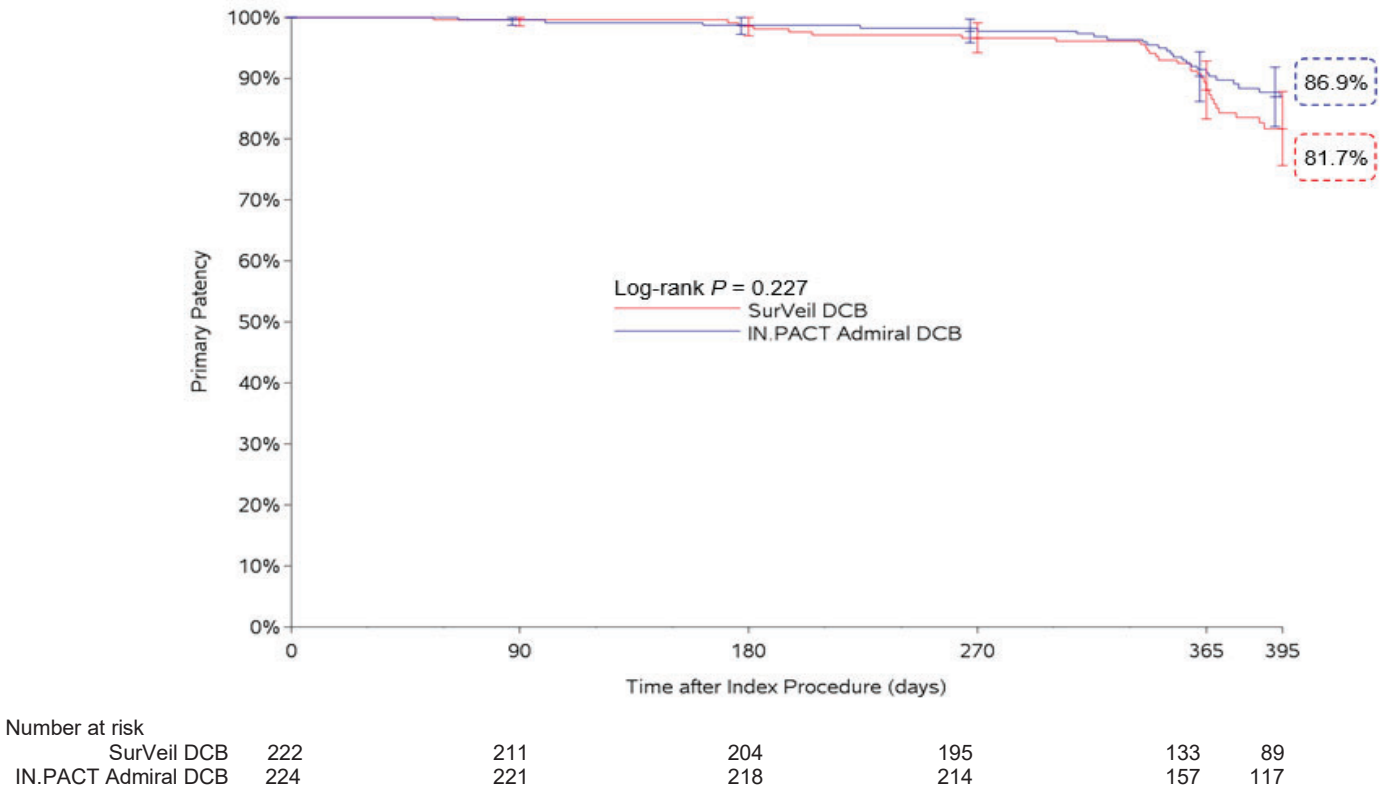


Figure 3. Kaplan-Meier Curve for Primary Patency to 395 days - ITT Analysis Population (N=446)

9.2.5.3 Secondary Endpoints

Secondary endpoints for the full ITT cohort for device/technical/procedure success, freedom from all-cause death, major target limb amputation and TVR through 30 days, target vessel patency (freedom from clinically driven TVR and freedom from binary restenosis), sustained clinical improvement, clinically driven TVR, historical MAEs, major target limb amputation, thrombosis at the target lesion, change in target limb Rutherford class from baseline, change in target limb PARC class from baseline, hemodynamic improvement as assessed by changes in resting target limb Ankle-Brachial Index (ABI) from baseline, change in Walking Impairment Questionnaire score from baseline, change in Six Minute Walk Test (6-MWT) from baseline, and change in Peripheral Artery Questionnaire (PAQ) from baseline were all evaluated.

Table 8. Secondary Endpoints – Clinical Endpoints through 12 Months - ITT Analysis Population (N=446

	SurVeil DCB (N=222 Subjects)	**IN.PACT Admiral DCB (N=224 Subjects)**
Freedom from all-cause death, major target limb amputation and TVR		
At 30 days	99.5% (217/218)	100.0% (223/223)
Target vessel patency[1]		
At 12 months	79.0% (139/176)	80.7% (159/197)
Sustained clinical improvement[2]		
At 6 months	75.6% (158/209)	77.5% (172/222)
At 12 months	61.1% (121/198)	63.9% (140/219)
Clinically-driven TLR		
At 6 months	1.4% (3/209)	1.4% (3/222)
At 12 months	5.6% (11/198)	4.7% (10/215)
Historical MAE[3]		
At 6 months	2.8% (6/212)	1.8% (4/223)
At 12 months	8.4% (17/203)	7.8% (17/219)
Major target limb amputation		
At 6 months	0.0% (0/208)	0.0% (0/222)
At 12 months	0.0% (0/196)	0.0% (0/215)
Thrombosis at the target lesion		
At 6 months	0.0% (0/208)	0.0% (0/222)
At 12 months	0.0% (0/196)	0.0% (0/215)

Denominators for 30-day outcomes include subjects with at least 28 days of follow-up or subjects experiencing the event through 30 days.

Denominators for 6-month outcomes include subjects with at least 150 days of follow-up or subjects experiencing the event through 180 days.

Denominators for 12-month outcomes include subjects with at least 335 days of follow-up or subjects experiencing the event through 365 days, with the exception of target vessel patency, where TVRs through **395** were counted.

[1] Target vessel patency, defined as freedom from clinically-driven TVR and freedom from binary restenosis restenosis defined as DUS PSVR ≥2.4 or ≥50% stenosis as assessed by independent angiographic and DUS core labs), within 12 months. No angiograms were used to determine binary restenosis.

[2] Sustained clinical improvement, defined as freedom from major target limb amputation, TVR and worsening target limb Rutherford class, within 6 and 12 months.

[3] Historical MAEs, defined as composite of all-cause death, clinically-driven TLR, major target limb amputation, or thrombosis at the target lesion, within 6 and 12 months.

Table 9. Change in Rutherford Classification from Baseline through 12 Months – ITT Analysis Population (N=446)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Change in Rutherford Classification from Baseline to 1 Month		
Grade ≥+3 Markedly improved	48.1% (101/210)	40.9% (90/220)
Grade +2 Moderately improved	30.0% (63/210)	35.5% (78/220)
Grade +1 Mildly improved	13.3% (28/210)	13.2% (29/220)
No change	7.6% (16/210)	9.1% (20/220)
Grade -1 Mildly worsening	0.5% (1/210)	0.9% (2/220)
Grade -2 Moderately worsening	0.0% (0/210)	0.0% (0/220)
Grade ≤-3 Markedly worsening	0.5% (1/210)	0.5% (1/220)
Change in Rutherford Classification from Baseline to 6 Months		
Grade ≥+3 Markedly improved	51.8% (101/195)	45.5% (95/209)
Grade +2 Moderately improved	33.3% (65/195)	33.5% (70/209)
Grade +1 Mildly improved	7.7% (15/195)	14.4% (30/209)
No change	5.6% (11/195)	5.7% (12/209)
Grade -1 Mildly worsening	0.5% (1/195)	1.0% (2/209)
Grade -2 Moderately worsening	0.5% (1/195)	0.0% (0/209)
Grade ≤-3 Markedly worsening	0.5% (1/195)	0.0% (0/209)
Change in Rutherford Classification from Baseline to 12 Months		
Grade ≥+3 Markedly improved	44.8% (82/183)	36.3% (74/204)
Grade +2 Moderately improved	27.3% (50/183)	37.3% (76/204)
Grade +1 Mildly improved	15.3% (28/183)	16.2% (33/204)
No change	9.8% (18/183)	7.8% (16/204)
Grade -1 Mildly worsening	2.7% (5/183)	1.5% (3/204)
Grade -2 Moderately worsening	0.0% (0/183)	1.0% (2/204)
Grade ≤-3 Markedly worsening	0.0% (0/183)	0.0% (0/204)

The denominator represents the number of subjects for whom Rutherford classification was available.

Table 10. Change in Target Limb PARC Clinical Symptom Classification from Baseline through 12 Months – ITT Analysis Population (N=446)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Change in PARC Classification from Baseline to 1 Month		
Grade ≥+3 Markedly improved	47.1% (99/210)	40.3% (89/221)
Grade +2 Moderately improved	28.1% (59/210)	35.3% (78/221)
Grade +1 Mildly improved	14.8% (31/210)	14.0% (31/221)
Grade 0 No change	8.6% (18/210)	8.1% (18/221)
Grade -1 Mildly worsening	1.0% (2/210)	1.8% (4/221)
Grade -2 Moderately worsening	0.0% (0/210)	0.0% (0/221)
Grade ≤-3 Markedly worsening	0.5% (1/210)	0.5% (1/221)
Change in PARC Classification from Baseline to 6 Months		
Grade ≥+3 Markedly improved	50.8% (99/195)	44.2% (92/208)
Grade +2 Moderately improved	33.3% (65/195)	33.7% (70/208)
Grade +1 Mildly improved	8.2% (16/195)	14.4% (30/208)
Grade 0 No change	6.2% (12/195)	6.7% (14/208)
Grade -1 Mildly worsening	0.5% (1/195)	1.0% (2/208)
Grade -2 Moderately worsening	0.5% (1/195)	0.0% (0/208)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Grade ≤-3 Markedly worsening	0.5% (1/195)	0.0% (0/208)
Change in PARC Classification from Baseline to 12 Months		
Grade ≥+3 Markedly improved	43.7% (80/183)	34.0% (69/203)
Grade +2 Moderately improved	29.0% (53/183)	39.4% (80/203)
Grade +1 Mildly improved	14.8% (27/183)	15.3% (31/203)
Grade 0 No change	9.3% (17/183)	8.4% (17/203)
Grade -1 Mildly worsening	3.3% (6/183)	2.0% (4/203)
Grade -2 Moderately worsening	0.0% (0/183)	0.5% (1/203)
Grade ≤-3 Markedly worsening	0.0% (0/183)	0.5% (1/203)
The denominator represents the number of subjects for whom PARC clinical classification was available.		

Table 11. Change in Ankle Brachial Index and Toe Brachial Index from Baseline through 12 Months – ITT Analysis Population (N=446)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Change from Baseline to 6 Months		
Resting ABI		
Mean ± SD (N)	0.2±0.2 (183)	0.2±0.2 (199)
Median (Q1, Q3)	0.2 (0.1,0.4)	0.2 (0.1,0.3)
Range (min, max)	(-0.5,0.8)	(-0.8,1.1)
Resting ABI reduction ≥0.15	3.3% (6/183)	4.0% (8/199)
Resting TBI		
Mean ± SD (N)	0.2±0.2 (9)	0.2±0.2 (10)
Median (Q1, Q3)	0.3 (-0.1,0.3)	0.1 (0.1,0.2)
Range (min, max)	(-0.1,0.4)	(-0.0,0.7)
Resting TBI reduction ≥0.15	0.0% (0/9)	0.0% (0/10)
Change from Baseline to 12 Months		
Resting ABI		
Mean ± SD (N)	0.2±0.2 (174)	0.2±0.2 (189)
Median (Q1, Q3)	0.2 (0.0,0.3)	0.2 (0.1,0.4)
Range (min, max)	(-0.4,0.8)	(-0.7,0.9)
Resting ABI reduction ≥0.15	8.6% (15/174)	3.2% (6/189)
Resting TBI		
Mean ± SD (N)	0.1±0.2 (11)	0.0±0.2 (8)
Median (Q1, Q3)	0.0 (-0.1,0.2)	0.1 (-0.0,0.2)
Range (min, max)	(-0.2,0.4)	(-0.4,0.3)
Resting TBI reduction ≥0.15	18.2% (2/11)	12.5% (1/8)
The denominator represents the number of subjects for whom the specific information was available.		

Table 12. Secondary Endpoints – Change in Walking Impairment Questionnaire from Baseline through 12 Months – ITT Analysis Population

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Change in WIQ Score from Baseline to 1 Month		
Walking Impairment Score		
Mean ± SD (N)	39.8±37.8 (204)	39.5±38.2 (219)
Median (Q1, Q3)	50.0 (25.0,75.0)	50.0 (25.0,75.0)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Range (min, max)	(-75.0,100.0)	(-75.0,100.0)
Walking Distance Score		
Mean ± SD (N)	34.2±40.0 (203)	28.9±39.1 (218)
Median (Q1, Q3)	37.6 (1.8,70.3)	23.4 (0.1,65.0)
Range (min, max)	(-90.6,99.4)	(-98.9,99.9)
Walking Speed Score		
Mean ± SD (N)	20.8±32.1 (198)	18.9±29.0 (215)
Median (Q1, Q3)	15.2 (0.0,43.5)	15.2 (0.0,34.8)
Range (min, max)	(-90.2,96.7)	(-81.5,100.0)
Stair Climbing Score		
Mean ± SD (N)	24.1±37.9 (200)	19.4±38.8 (217)
Median (Q1, Q3)	20.8 (0.0,54.2)	12.5 (0.0,45.8)
Range (min, max)	(-100.0,95.8)	(-100.0,100.0)
Change in WIQ Score from Baseline to 12 Months		
Walking Impairment Score		
Mean ± SD (N)	34.3±42.3 (181)	38.3±42.0 (205)
Median (Q1, Q3)	25.0 (0.0,75.0)	50.0 (25.0,75.0)
Range (min, max)	(-75.0,100.0)	(-75.0,100.0)
Walking Distance Score		
Mean ± SD (N)	29.9±38.2 (181)	30.9±40.3 (204)
Median (Q1, Q3)	26.3 (0.0,62.9)	27.7 (1.1,66.9)
Range (min, max)	(-89.5,99.4)	(-98.2,100.0)
Walking Speed Score		
Mean ± SD (N)	19.2±33.4 (178)	21.2±34.7 (205)
Median (Q1, Q3)	17.4 (0.0,43.5)	17.4 (0.0,43.5)
Range (min, max)	(-87.0,96.7)	(-96.7,100.0)
Stair Climbing Score		
Mean ± SD (N)	20.7±38.0 (180)	24.1±40.5 (205)
Median (Q1, Q3)	20.8 (-4.2,47.9)	20.8 (0.0,54.2)
Range (min, max)	(-100.0,100.0)	(-100.0,100.0)

The denominator represents the number of subjects for whom the specific score was available.

Table 13. Analysis of Secondary Endpoints – Change in 6-minute Walk Test from Baseline to 12 Months - ITT Analysis Population

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
Change in 6-MWT from Baseline to 12 Months		
Walking Distance (m)		
Mean ± SD (N)	45.8±118.8 (163)	60.7±113.6 (180)
Median (Q1, Q3)	44.0 (-10.0,108.2)	45.3 (-5.0,125.4)
Range (min, max)	(-233.0,692.1)	(-234.1,500.0)

The denominator represents the number of subjects for whom the specific information was available.

Table 14. Secondary Endpoints – Improvement in Peripheral Artery Questionnaire Scores from Baseline through 12 Months – ITT Analysis Population (N=446)

	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)
1 Month		
Physical Function Score Improvement	78.7% (140/178)	81.6% (160/196)
Stability Score Improvement	74.9% (152/203)	75.8% (166/219)
Symptom Score Improvement	85.2% (173/203)	84.5% (185/219)
Treatment Satisfaction Score Improvement	34.7% (70/202)	36.5% (80/219)
Quality of Life Score Improvement	84.2% (171/203)	86.8% (190/219)
Social Limitation Score Improvement	76.3% (135/177)	81.2% (164/202)
Summary Score Improvement	89.2% (181/203)	90.0% (197/219)
12 Months		
Physical Function Score Improvement	75.8% (122/161)	79.2% (141/178)
Stability Score Improvement	41.1% (74/180)	42.4% (87/205)
Symptom Score Improvement	82.2% (148/180)	80.5% (165/205)
Treatment Satisfaction Score Improvement	34.6% (62/179)	34.6% (71/205)
Quality of Life Score Improvement	85.6% (154/180)	82.4% (169/205)
Social Limitation Score Improvement	75.9% (123/162)	75.4% (138/183)
Summary Score Improvement	86.1% (155/180)	83.4% (171/205)

Improvement is defined as increase in score of >0.

9.2.5.4 Summary of Adverse Events

Table 15 displays the rates of site reported Serious Adverse Events (SAEs) classified by the MedDRA System Organ Class (SOC) and preferred term. An SAE was defined as an adverse event that leads to:

1. Death
2. A serious deterioration in the health of the subject that either results in:
    a. life-threatening illness or injury or
    b. a permanent impairment of a body structure or a body function or
    c. in-patient hospitalization or prolongation of existing hospitalization or
    d. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
3. Fetal distress, fetal death, or congenital abnormality or birth defect.

Table 15. Summary of All Site-Reported Serious Adverse Events through 12 Months –ITT Analysis Population (N=446)

	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
Serious Adverse Events	**Events**	**Rate of Subjects with Event**	**Events**	**Rate of Subjects with Event**
Any Serious Adverse Event	**176**	**44.6% (99/222)**	**193**	**37.9% (85/224)**
Blood and lymphatic system disorders	**6**	**2.7% (6/222)**	**1**	**0.4% (1/224)**
Anaemia	2	0.9% (2/222)	1	0.4% (1/224)
Haemorrhagic anaemia	3	1.4% (3/222)	0	0.0% (0/224)
Microcytic anaemia	1	0.5% (1/222)	0	0.0% (0/224)

Serious Adverse Events	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Cardiac disorders	**27**	**9.5% (21/222)**	**31**	**10.7% (24/224)**
Acute myocardial infarction	5	2.3% (5/222)	7	3.1% (7/224)
Angina pectoris	4	1.8% (4/222)	2	0.9% (2/224)
Angina unstable	2	0.9% (2/222)	1	0.4% (1/224)
Aortic valve stenosis	0	0.0% (0/222)	1	0.4% (1/224)
Atrial fibrillation	1	0.5% (1/222)	1	0.4% (1/224)
Atrial flutter	1	0.5% (1/222)	1	0.4% (1/224)
Atrioventricular block	0	0.0% (0/222)	1	0.4% (1/224)
Atrioventricular block second degree	0	0.0% (0/222)	2	0.9% (2/224)
Cardiac arrest	1	0.5% (1/222)	2	0.9% (2/224)
Cardiac failure	0	0.0% (0/222)	1	0.4% (1/224)
Cardiac failure acute	0	0.0% (0/222)	1	0.4% (1/224)
Cardiac failure congestive	8	1.8% (4/222)	3	1.3% (3/224)
Coronary artery disease	1	0.5% (1/222)	3	0.4% (1/224)
Coronary artery occlusion	0	0.0% (0/222)	1	0.4% (1/224)
Coronary artery stenosis	2	0.9% (2/222)	1	0.4% (1/224)
Myocardial ischaemia	1	0.5% (1/222)	0	0.0% (0/224)
Sinus node dysfunction	0	0.0% (0/222)	1	0.4% (1/224)
Ventricular extrasystoles	1	0.5% (1/222)	0	0.0% (0/224)
Ventricular fibrillation	0	0.0% (0/222)	2	0.9% (2/224)
Eye disorders	**2**	**0.9% (2/222)**	**1**	**0.4% (1/224)**
Glaucoma	1	0.5% (1/222)	0	0.0% (0/224)
Retinal artery occlusion	0	0.0% (0/222)	1	0.4% (1/224)
Vitreous haemorrhage	1	0.5% (1/222)	0	0.0% (0/224)
Gastrointestinal disorders	**7**	**2.3% (5/222)**	**10**	**4.0% (9/224)**
Abdominal hernia	1	0.5% (1/222)	0	0.0% (0/224)
Barrett's oesophagus	0	0.0% (0/222)	1	0.4% (1/224)
Dysphagia	0	0.0% (0/222)	1	0.4% (1/224)
Gastric ulcer haemorrhage	0	0.0% (0/222)	1	0.4% (1/224)
Gastritis	0	0.0% (0/222)	1	0.4% (1/224)
Gastrointestinal haemorrhage	3	0.9% (2/222)	1	0.4% (1/224)
Inguinal hernia	0	0.0% (0/222)	1	0.4% (1/224)
Intestinal obstruction	1	0.5% (1/222)	0	0.0% (0/224)
Lower gastrointestinal haemorrhage	0	0.0% (0/222)	1	0.4% (1/224)
Nausea	0	0.0% (0/222)	1	0.4% (1/224)
Retroperitoneal fibrosis	1	0.5% (1/222)	0	0.0% (0/224)
Umbilical hernia	1	0.5% (1/222)	1	0.4% (1/224)
Vomiting	0	0.0% (0/222)	1	0.4% (1/224)
General disorders and administration site conditions	**12**	**5.0% (11/222)**	**7**	**2.7% (6/224)**
Catheter site discharge	2	0.9% (2/222)	0	0.0% (0/224)
Catheter site haematoma	3	1.4% (3/222)	0	0.0% (0/224)
Catheter site haemorrhage	0	0.0% (0/222)	1	0.4% (1/224)
Death	1	0.5% (1/222)[1]	0	0.0% (0/224)
Drug withdrawal syndrome	1	0.5% (1/222)	0	0.0% (0/224)
Fatigue	0	0.0% (0/222)	1	0.4% (1/224)

Serious Adverse Events	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Non-cardiac chest pain	3	1.4% (3/222)	2	0.4% (1/224)
Pyrexia	0	0.0% (0/222)	1	0.4% (1/224)
Vascular stent occlusion	1	0.5% (1/222)	1	0.4% (1/224)
Vascular stent restenosis	1	0.5% (1/222)	1	0.4% (1/224)
Hepatobiliary disorders	**1**	**0.5% (1/222)**	**0**	**0.0% (0/224)**
Cholelithiasis	1	0.5% (1/222)	0	0.0% (0/224)
Immune system disorders	**1**	**0.5% (1/222)**	**1**	**0.4% (1/224)**
Anaphylactic reaction	1	0.5% (1/222)	1	0.4% (1/224)
Infections and infestations	**16**	**6.3% (14/222)**	**24**	**5.8% (13/224)**
Bronchitis	0	0.0% (0/222)	2	0.4% (1/224)
Bronchitis bacterial	0	0.0% (0/222)	1	0.4% (1/224)
Cellulitis	1	0.5% (1/222)	0	0.0% (0/224)
Diverticulitis	0	0.0% (0/222)	1	0.4% (1/224)
Endocarditis bacterial	0	0.0% (0/222)	1	0.4% (1/224)
Enterococcal bacteraemia	0	0.0% (0/222)	1	0.4% (1/224)
Epididymitis	1	0.5% (1/222)	0	0.0% (0/224)
Gastroenteritis	0	0.0% (0/222)	1	0.4% (1/224)
Infected skin ulcer	0	0.0% (0/222)	1	0.4% (1/224)
Infection	1	0.5% (1/222)	0	0.0% (0/224)
Infective exacerbation of chronic obstructive airways disease	0	0.0% (0/222)	1	0.4% (1/224)
Influenza	0	0.0% (0/222)	1	0.4% (1/224)
Localised infection	0	0.0% (0/222)	1	0.4% (1/224)
Lung infection	1	0.5% (1/222)	0	0.0% (0/224)
Osteomyelitis	0	0.0% (0/222)	1	0.4% (1/224)
Pneumonia	6	2.7% (6/222)	8	2.7% (6/224)
Postoperative wound infection	1	0.5% (1/222)	0	0.0% (0/224)
Pyelonephritis	1	0.5% (1/222)	0	0.0% (0/224)
Pyelonephritis acute	1	0.5% (1/222)	0	0.0% (0/224)
Sepsis	1	0.5% (1/222)	2	0.9% (2/224)
Septic shock	0	0.0% (0/222)	1	0.4% (1/224)
Staphylococcal infection	1	0.5% (1/222)	0	0.0% (0/224)
Urinary tract infection	1	0.5% (1/222)	0	0.0% (0/224)
Wound infection	0	0.0% (0/222)	1	0.4% (1/224)
Injury, poisoning and procedural complications	**22**	**9.0% (20/222)**	**16**	**6.7% (15/224)**
Ankle fracture	2	0.9% (2/222)	0	0.0% (0/224)
Arterial bypass thrombosis	0	0.0% (0/222)	1	0.4% (1/224)
Femoral neck fracture	1	0.5% (1/222)	2	0.9% (2/224)
Hip fracture	1	0.5% (1/222)	0	0.0% (0/224)
Meniscus injury	0	0.0% (0/222)	1	0.4% (1/224)
Overdose	1	0.5% (1/222)	0	0.0% (0/224)
Peripheral artery restenosis	9	3.6% (8/222)	6	2.2% (5/224)
Procedural hypotension	1	0.5% (1/222)	0	0.0% (0/224)
Pubis fracture	0	0.0% (0/222)	1	0.4% (1/224)
Rib fracture	1	0.5% (1/222)	0	0.0% (0/224)
Scar	0	0.0% (0/222)	1	0.4% (1/224)

Serious Adverse Events	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Spinal compression fracture	0	0.0% (0/222)	1	0.4% (1/224)
Transplant failure	0	0.0% (0/222)	1	0.4% (1/224)
Upper limb fracture	1	0.5% (1/222)	0	0.0% (0/224)
Vascular access site pseudoaneurysm	3	1.4% (3/222)	2	0.9% (2/224)
Vascular pseudoaneurysm	2	0.9% (2/222)	0	0.0% (0/224)
Investigations	**0**	**0.0% (0/222)**	**1**	**0.4% (1/224)**
Blood pressure systolic increased	0	0.0% (0/222)	1	0.4% (1/224)
Metabolism and nutrition disorders	**2**	**0.9% (2/222)**	**3**	**0.4% (1/224)**
Dehydration	0	0.0% (0/222)	2	0.4% (1/224)
Hyperkalaemia	0	0.0% (0/222)	1	0.4% (1/224)
Hyperlipidaemia	1	0.5% (1/222)	0	0.0% (0/224)
Hypoglycaemia	1	0.5% (1/222)	0	0.0% (0/224)
Musculoskeletal and connective tissue disorders	**7**	**3.2% (7/222)**	**11**	**4.9% (11/224)**
Arthralgia	1	0.5% (1/222)	0	0.0% (0/224)
Back disorder	0	0.0% (0/222)	1	0.4% (1/224)
Back pain	0	0.0% (0/222)	1	0.4% (1/224)
Compartment syndrome	0	0.0% (0/222)	1	0.4% (1/224)
Dupuytren's contracture	1	0.5% (1/222)	0	0.0% (0/224)
Haemarthrosis	0	0.0% (0/222)	1	0.4% (1/224)
Intervertebral disc protrusion	1	0.5% (1/222)	0	0.0% (0/224)
Lumbar spinal stenosis	1	0.5% (1/222)	2	0.9% (2/224)
Muscle spasms	1	0.5% (1/222)	0	0.0% (0/224)
Osteoarthritis	0	0.0% (0/222)	1	0.4% (1/224)
Pain in extremity	1	0.5% (1/222)	2	0.9% (2/224)
Rotator cuff syndrome	0	0.0% (0/222)	1	0.4% (1/224)
Spinal osteoarthritis	1	0.5% (1/222)	0	0.0% (0/224)
Spondylolysis	0	0.0% (0/222)	1	0.4% (1/224)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**4**	**1.8% (4/222)**	**6**	**2.7% (6/224)**
Carcinoid tumour of the small bowel	0	0.0% (0/222)	1	0.4% (1/224)
Cholesteatoma	1	0.5% (1/222)	0	0.0% (0/224)
Gastrooesophageal cancer	0	0.0% (0/222)	1	0.4% (1/224)
Laryngeal cancer metastatic	0	0.0% (0/222)	1	0.4% (1/224)
Lung neoplasm malignant	1	0.5% (1/222)	0	0.0% (0/224)
Neoplasm skin	0	0.0% (0/222)	1	0.4% (1/224)
Papillary thyroid cancer	0	0.0% (0/222)	1	0.4% (1/224)
Salivary gland neoplasm	1	0.5% (1/222)	0	0.0% (0/224)
Squamous cell carcinoma	1	0.5% (1/222)	0	0.0% (0/224)
Squamous cell carcinoma of lung	0	0.0% (0/222)	1	0.4% (1/224)
Nervous system disorders	**8**	**3.2% (7/222)**	**10**	**4.0% (9/224)**
Carotid artery stenosis	1	0.5% (1/222)	2	0.9% (2/224)
Cerebrovascular accident	0	0.0% (0/222)	1	0.4% (1/224)
Embolic stroke	1	0.5% (1/222)	1	0.4% (1/224)
Encephalopathy	0	0.0% (0/222)	2	0.9% (2/224)
Epidural lipomatosis	1	0.5% (1/222)	0	0.0% (0/224)
Haemorrhagic stroke	1	0.5% (1/222)	0	0.0% (0/224)

Serious Adverse Events	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Metabolic encephalopathy	0	0.0% (0/222)	3	1.3% (3/224)
Post herpetic neuralgia	1	0.5% (1/222)	0	0.0% (0/224)
Presyncope	1	0.5% (1/222)	1	0.4% (1/224)
Syncope	1	0.5% (1/222)	0	0.0% (0/224)
Transient ischaemic attack	1	0.5% (1/222)	0	0.0% (0/224)
Product issues	**0**	**0.0% (0/222)**	**1**	**0.4% (1/224)**
Device malfunction	0	0.0% (0/222)	1	0.4% (1/224)
Psychiatric disorders	**0**	**0.0% (0/222)**	**2**	**0.9% (2/224)**
Completed suicide	0	0.0% (0/222)	1	0.4% (1/224)
Mental disorder	0	0.0% (0/222)	1	0.4% (1/224)
Renal and urinary disorders	**3**	**1.4% (3/222)**	**4**	**1.8% (4/224)**
Acute kidney injury	1	0.5% (1/222)	3	1.3% (3/224)
Chronic kidney disease	0	0.0% (0/222)	1	0.4% (1/224)
Nephrolithiasis	1	0.5% (1/222)	0	0.0% (0/224)
Renal mass	1	0.5% (1/222)	0	0.0% (0/224)
Reproductive system and breast disorders	**1**	**0.5% (1/222)**	**1**	**0.4% (1/224)**
Genital erosion	1	0.5% (1/222)	0	0.0% (0/224)
Vaginal prolapse	0	0.0% (0/222)	1	0.4% (1/224)
Respiratory, thoracic and mediastinal disorders	**3**	**1.4% (3/222)**	**17**	**4.0% (9/224)**
Acute respiratory failure	0	0.0% (0/222)	3	1.3% (3/224)
Aspiration	1	0.5% (1/222)	0	0.0% (0/224)
Chronic obstructive pulmonary disease	1	0.5% (1/222)	4	0.4% (1/224)
Dyspnoea	1	0.5% (1/222)	1	0.4% (1/224)
Emphysema	0	0.0% (0/222)	1	0.4% (1/224)
Epistaxis	0	0.0% (0/222)	2	0.4% (1/224)
Hypoxia	0	0.0% (0/222)	1	0.4% (1/224)
Pulmonary mass	0	0.0% (0/222)	1	0.4% (1/224)
Respiratory failure	0	0.0% (0/222)	4	1.3% (3/224)
Skin and subcutaneous tissue disorders	**1**	**0.5% (1/222)**	**0**	**0.0% (0/224)**
Neuropathic ulcer	1	0.5% (1/222)	0	0.0% (0/224)
Vascular disorders	**53**	**18.9% (42/222)**	**46**	**15.2% (34/224)**
Aortic aneurysm	1	0.5% (1/222)	1	0.4% (1/224)
Arterial spasm	1	0.5% (1/222)	0	0.0% (0/224)
Arteriovenous fistula	0	0.0% (0/222)	1	0.4% (1/224)
Deep vein thrombosis	1	0.5% (1/222)	1	0.4% (1/224)
Haematoma	1	0.5% (1/222)	0	0.0% (0/224)
Haemorrhage	1	0.5% (1/222)	0	0.0% (0/224)
Hypertension	1	0.5% (1/222)	0	0.0% (0/224)
Hypertensive emergency	0	0.0% (0/222)	1	0.4% (1/224)
Hypotension	1	0.5% (1/222)	1	0.4% (1/224)
Iliac artery occlusion	0	0.0% (0/222)	1	0.4% (1/224)
Orthostatic hypotension	0	0.0% (0/222)	1	0.4% (1/224)
Peripheral arterial occlusive disease	2	0.9% (2/222)	2	0.9% (2/224)
Peripheral artery aneurysm	3	0.5% (1/222)	0	0.0% (0/224)
Peripheral artery dissection	1	0.5% (1/222)	1	0.4% (1/224)

Serious Adverse Events	SurVeil DCB (N=222 Subjects)		IN.PACT Admiral DCB (N=224 Subjects)	
	Events	Rate of Subjects with Event	Events	Rate of Subjects with Event
Peripheral artery occlusion	12	4.5% (10/222)	17	5.8% (13/224)
Peripheral artery stenosis	23	9.9% (22/222)	15	5.4% (12/224)
Peripheral embolism	1	0.5% (1/222)	1	0.4% (1/224)
Peripheral ischaemia	1	0.5% (1/222)	0	0.0% (0/224)
Peripheral vascular disorder	1	0.5% (1/222)	0	0.0% (0/224)
Peripheral venous disease	0	0.0% (0/222)	1	0.4% (1/224)
Subclavian steal syndrome	0	0.0% (0/222)	1	0.4% (1/224)
Varicose vein	2	0.5% (1/222)	1	0.4% (1/224)

This table presents serious adverse events starting from the index procedure through 365 days post procedure.

[1] Subject 009-005 expired at home of unknown cause.

9.2.5.5 Subgroup Analyses

The TRANSCEND study results have been analyzed by different pre-defined sub-groups to investigate the consistency of results through 12 months. The primary safety endpoint at 12 months (Table 16) and primary efficacy of primary patency at 12 months (Table 17) are illustrated for each subgroup in the tables below. Primary safety endpoint results were consistent across all subgroups except for the age subgroup, where results differed between subjects younger than 65 years and subjects older than 65 years (P=0.0624 <0.15; the prespecified level of significance for the subgroup analysis was 0.15). Primary effectiveness endpoint results were consistent across all subgroups as evidenced by P for interaction >0.15.

Table 16. Subgroup Analysis: Primary Safety Endpoint - ITT Analysis Population (N=446)

Primary Safety Endpoint	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)	Difference [95% CI]	P-value for Interaction of Treatment and Subgroup[1]
Age				0.0624
Age ≤65	87.0% (60/69)	91.6% (87/95)	-4.6% [-14.3%,5.1%]	
Age >65	94.6% (123/130)	88.5% (108/122)	6.1% [-0.8%,12.9%]	
Smoking				0.2576
Current smoker	95.1% (78/82)	89.0% (73/82)	6.1% [-2.1%,14.3%]	
Former smoker	90.7% (78/86)	88.9% (88/99)	1.8% [-6.9%,10.5%]	
Never smoked	87.1% (27/31)	94.4% (34/36)	-7.3% [-21.3%,6.6%]	
Gender				0.6976
Male	92.6% (113/122)	89.7% (122/136)	2.9% [-4.0%,9.8%]	
Female	90.9% (70/77)	90.1% (73/81)	0.8% [-8.3%,9.9%]	
Diabetes Mellitus				0.5935
Diabetics	89.4% (76/85)	88.6% (78/88)	0.8% [-8.5%,10.1%]	
Non-diabetics	93.9% (107/114)	90.7% (117/129)	3.2% [-3.5%,9.8%]	
Chronic Renal Insufficiency				0.6561
Chronic renal insufficiency	95.5% (42/44)	91.7% (22/24)	3.8% [-8.9%,16.4%]	
Non-chronic renal insufficiency	91.0% (141/155)	89.6% (172/192)	1.4% [-4.9%,7.6%]	
Lesion Length				0.4027
Total lesion length ≤90mm	93.3% (112/120)	93.5% (129/138)	-0.1% [-6.2%,5.9%]	
Total lesion length >90mm	89.9% (71/79)	83.5% (66/79)	6.3% [-4.2%,16.9%]	
Lesion Calcification[2]				0.3226
None/mildly calcified	91.3% (94/103)	92.2% (94/102)	-0.9% [-8.4%,6.7%]	
Moderately/severely calcified	92.7% (89/96)	87.7% (100/114)	5.0% [-3.0%,12.9%]	
Lesion Type				0.9719
de novo lesion	92.2% (177/192)	89.6% (189/211)	2.6% [-3.0%,8.2%]	
Restenotic lesion	85.7% (6/7)	100.0% (6/6)	-14.3% [-40.2%,11.6%]	
Bailout Stenting				0.5923
Subjects with bailout stents	93.8% (15/16)	85.7% (12/14)	8.0% [-13.8%,29.9%]	
Subjects without bailout stents	91.8% (168/183)	90.1% (183/203)	1.7% [-4.1%,7.4%]	
Residual Stenosis after Pre-dilatation				0.9132
<50%	92.7% (140/151)	90.7% (146/161)	2.0% [-4.1%,8.1%]	
≥50%	89.7% (35/39)	86.0% (43/50)	3.7% [-9.8%,17.3%]	

[1] P-value is derived from logistic regression on the primary safety endpoint with treatment, subgroup, and interaction of treatment and subgroup as covariates.

[2] Calcification is based on angiographic core laboratory data.

Table 17. Subgroup Analysis: Primary Effectiveness Endpoint - ITT Analysis Population (N=446)

Primary Effectiveness Endpoint	SurVeil DCB (N=222 Subjects)	IN.PACT Admiral DCB (N=224 Subjects)	Difference [95% CI]	P-value for Interaction of Treatment and Subgroup[1]
Age				0.4973
Age ≤65	82.3% (51/62)	89.3% (75/84)	-7.0% [-18.6%,4.6%]	
Age >65	82.2% (88/107)	84.6% (88/104)	-2.4% [-12.4%,7.7%]	
Smoking				0.9977
Current smoker	86.3% (63/73)	90.1% (64/71)	-3.8% [-14.3%,6.7%]	
Former smoker	81.4% (57/70)	86.7% (72/83)	-5.3% [-17.0%,6.4%]	
Never smoked	73.1% (19/26)	79.4% (27/34)	-6.3% [-28.1%,15.5%]	
Gender				0.7177
Male	82.9% (87/105)	88.1% (104/118)	-5.3% [-14.6%,4.0%]	
Female	81.3% (52/64)	84.3% (59/70)	-3.0% [-15.8%,9.8%]	
Diabetes Mellitus				0.6602
Diabetics	72.7% (48/66)	81.1% (60/74)	-8.4% [-22.3%,5.6%]	
Non-diabetics	88.3% (91/103)	90.4% (103/114)	-2.0% [-10.2%,6.2%]	
Chronic Renal Insufficiency				0.9681
Chronic renal insufficiency	81.6% (31/38)	86.4% (19/22)	-4.8% [-23.7%,14.1%]	
Non-chronic renal insufficiency	82.4% (108/131)	86.7% (143/165)	-4.2% [-12.6%,4.1%]	
Lesion Length				0.6228
Total lesion length ≤90mm	88.5% (92/104)	90.1% (109/121)	-1.6% [-9.7%,6.5%]	
Total lesion length >90mm	72.3% (47/65)	80.6% (54/67)	-8.3% [-22.7%,6.1%]	
Lesion Calcification[2]				0.8860
None/mildly calcified	82.6% (76/92)	86.5% (77/89)	-3.9% [-14.4%,6.6%]	
Moderately/severely calcified	81.8% (63/77)	86.9% (86/99)	-5.1% [-15.9%,5.8%]	
Lesion Type				0.2236
de novo lesion	84.0% (136/162)	86.8% (158/182)	-2.9% [-10.4%,4.6%]	
Restenotic lesion	42.9% (3/7)	83.3% (5/6)	-40.5% [-87.7%,6.8%]	
Bailout Stenting				0.7828
Subjects with bailout stents	84.6% (11/13)	91.7% (11/12)	-7.1% [-32.1%,18.0%]	
Subjects without bailout stents	82.1% (128/156)	86.4% (152/176)	-4.3% [-12.2%,3.6%]	
Residual Stenosis after Pre-dilatation				0.9893
<50%	84.9% (107/126)	87.9% (123/140)	-2.9% [-11.2%,5.3%]	
≥50%	77.1% (27/35)	81.4% (35/43)	-4.3% [-22.4%,13.9%]	

[1] P-value is derived from logistic regression on the primary effectiveness endpoint with treatment, subgroup, and interaction of treatment and subgroup as covariates.

[2] Calcification is based on angiographic core laboratory data.

9.3 Late Mortality

The TRANSCEND trial is ongoing through 5 years, and in order to demonstrate that the SurVeil DCB does not represent an unacceptable risk of late mortality compared to the currently marketed IN.PACT Admiral DCB, additional exploratory analyses were performed including: 1) Bayesian predictive modeling to estimate 2- and 3-year mortality rates (Table 18) and 2) Kaplan-Meier (KM) analyses (Table 19). Both analyses were conducted based on all available data. Vital status is known at a time point if a subject completed the visit for that time point or later, or if a vitality assessment was completed for an exited subject confirming the subject was alive beyond that time point, or if the subject died prior to the time point. The analysis data set included data through June 30, 2022.

Table 18. TRANSCEND Predictive Mortality Analysis Vital Status

Time	SurVeil DCB (n)		IN.PACT Admiral DCB (n)		Total (n)	
	Unknown	Known	Unknown	Known	Unknown	Known
Randomization	0	222	0	224	0	446
6-Months (180 days)	2	220	0	224	2	444
1-Year (365 days)	4	218	0	224	4	442
2-Years (730 days)	8	214	1	223	9	437
3-Years (1095 days)	12	170	5	189	17	359

Table 19. Kaplan Meier Analysis

	Time after Procedure (days)				
All-Cause Survival	**0**	**180**	**365**	**730**	**1095**
SurVeil DCB					
# Entered	222	216	212	200	156
# Censored	-	2	3	4	42
# Events	-	4	7	18	24
Survival Rate [%]	-	98.2%	96.8%	91.8%	89.0%
Greenwood SE [%]	-	0.90%	1.19%	1.86%	2.13%
95% Confidence Interval[1]	-	[96.4, 100.0%]	[94.5, 99.2%]	[88.2, 95.5%]	[84.9, 93.2%]
IN.PACT Admiral DCB					
# Entered	224	223	217	208	164
# Censored	-	0	0	0	33
# Events	-	1	7	16	27
Survival Rate [%]	-	99.6%	96.9%	92.9%	87.8%
Greenwood SE [%]	-	0.45%	1.16%	1.72%	2.21%
95% Confidence Interval[1]	-	[98.7, 100.0%]	[94.6, 99.2%]	[89.5, 96.3%]	[83.5, 92.2%]

[1] Log Confidence Intervals

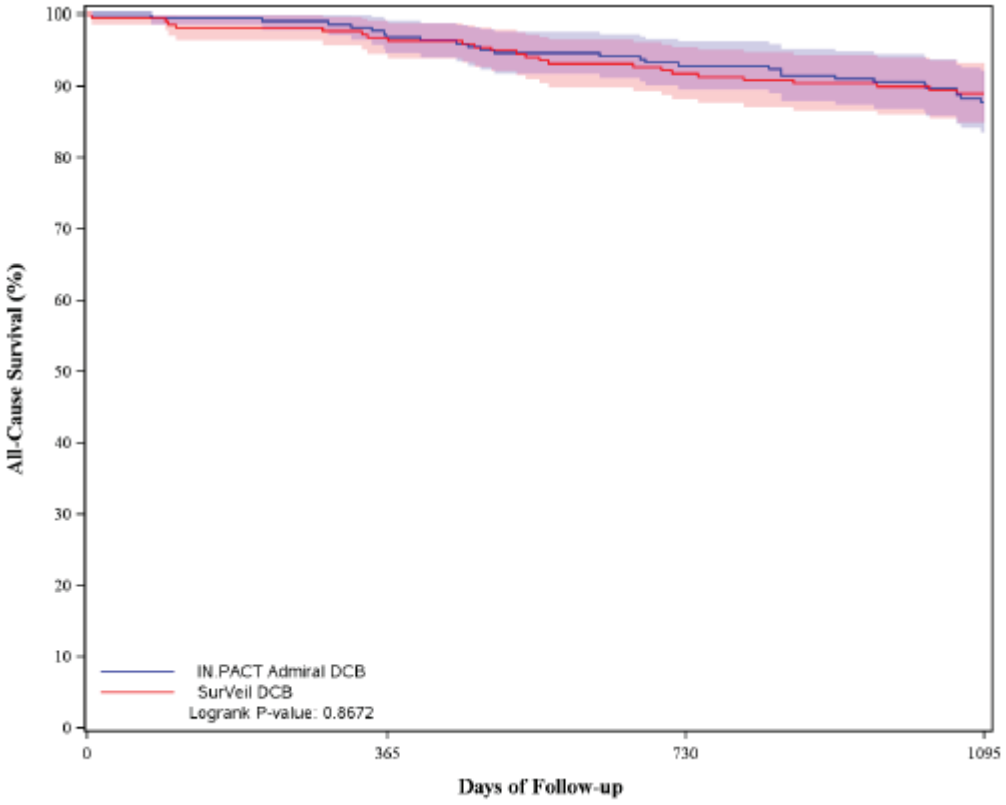


Figure 4. Kaplan-Meier estimates of survival through 3 years by arm

Bayesian Predictive Modeling:

A Bayesian piecewise constant hazard model was used for estimation and prediction of unobserved survival times through 3 years comparing the SurVeil DCB arm to the IN.PACT Admiral DCB arm from the TRANSCEND trial. The predictions of survival are based on Kaplan-Meier estimates of 2-and 3-year survival calculated with observed and predicted future data for the randomized groups. The Kaplan Meier estimate of the survival rate was 91.8% and 89.0% in the SurVeil DCB group and 92.9% and 87.8% in the IN.PACT Admiral DCB group at 2 and 3 years, respectively. For both the 2-and 3-year, the predictive analysis demonstrates that the mortality risk of the SurVeil DCB treatment group is comparable to that of the IN.PACT Admiral DCB group.

Based on the totality of the data provided, the SurVeil DCB does not appear to present an unacceptable mortality risk at 3-year, compared to currently marketed paclitaxel-coated device IN.PACT Admiral DCB.

9.4 PREVEIL Early Feasibility Study - Pharmacokinetics

A prospective, multicenter, single-arm trial to assess the pharmacokinetics of the Surmodics Drug-Coated Balloon in the treatment of subjects with de novo lesions of the femoropopliteal artery was conducted. The pharmacokinetic (PK) profile of paclitaxel following treatment with SurVeil DCB was evaluated in 13 patients (9 male, 4 female) receiving 1300 – 3800 µg of paclitaxel. The primary end point was peak plasma paclitaxel concentrations post-index DCB procedure. Plasma paclitaxel levels were assessed at baseline,

immediately post-index procedure and at 1,2,4, and 12 hours (or open discharge), and 30 days post-index procedure. Secondary performance endpoints include “area under the drug concentration time curve (AUC)”, as measured from the time of intervention to the time when the paclitaxel level was no longer quantifiable. The lower limit of quantification of paclitaxel in the plasma was 0.1 ng/mL. The average lesion length for PK study was 56.38 mm ± 32.67 mm (n=13). Mean plasma concentration peaked immediately post-procedure (C_{max} 2.25 ± 2.5 ng/mL) and was undetectable at 30 days. The $AUC_{0\text{-last}}$ was 3.74 ± 3.2 hr*ng/mL. These data indicate that treatment with the SurVeil DCB provides low systemic exposure of paclitaxel. A summary of the pharmacokinetics parameters is presented in the following table:

Table 20. Summary of Pharmacokinetic Parameters

Enrolled Subjects (N=13)*	Peak Paclitaxel Concentration (C_{max}) (ng/mL)	Dose-Normalized Peak Paclitaxel Concentration (C_{max}/Dose) (ng/mL/mg)	AUC_{last} (ng*hr/mL)	Dose-Normalized AUC_{last}/Dose) (ng*hr/mL/mg)
Mean ± SD (N)	2.25 ± 2.5 (10)	0.679 ± 0.672 (10)	3.74 ± 3.2 (10)	1.18 ± 0.889 (10)
95% CI (Lower, Upper)	-3.42, 7.91	-0.840, 2.20	-3.49, 11.0	-0.830, 3.19
Median (25%tile, 75%tile)	1.22 (0.472, 3.10)	0.431 (0.155, 0.974)	2.94 (1.33, 5.45)	0.889 (0.504, 2.03)
Range (min, max)	(0.235, 8.24)	(0.0935, 2.19)	(0.383, 11)	(0.153, 2.93)

NOTE: Three (3) subjects had insufficient data to complete PK analysis and were excluded from descriptive statistics.

10 HOW SUPPLIED

STERILE: This device is sterilized by electron beam radiation. Do not use if package is opened or damaged. This is device is intended for single use only. Do not resterilize.

CONTENTS: One (1) SurVeil DCB catheter.

STORAGE: Store in its original container with labeling. Store at 25°C (77°F); excursions permitted to 15°C - 30°C (59°F - 86°F). Use prior to the use by date. Do not expose to organic solvents (e.g. alcohol), ionizing radiation or ultraviolet light.

11 INSTRUCTIONS FOR USE

11.1 Required Materials

To safely perform a procedure using the SurVeil DCB, the following materials are required:

- 0.035 inch (0.89 mm) guidewire
- Contrast solution
- Sterile saline
- Inflation device with manometer
- Luer lock syringe
- Introducer/guide sheath
- Pre-dilatation PTA balloon catheter

11.2 Recommended tools

- 3-Way stopcock
- Torque device

11.3 Inspection prior to use

Examine all equipment to be used during the procedure to verify proper function. Carefully inspect sterile package before opening to verify that the sterile package and the SurVeil DCB have not been damaged.

Warning: Do not use if the integrity of the sterile package has been compromised or if any sterile package or product defects are noted.

11.4 Preparation

1. Prepare the inflation device, introducer sheath, and guidewire according to manufacturer's instructions. Prepare vascular access site according to standard practice.
2. Perform pre-dilatation inflation of the target vessel with a balloon dilatation catheter inflated to approximately 1 mm less than the reference vessel diameter (RVD).

NOTE: Appropriate vessel preparation is required prior to the use of the SurVeil DCB. Vessel preparation using only pre-dilatation was studied in the clinical study. Other methods of preparation, such as atherectomy, have not been studied.

11.5 Prepare SurVeil DCB for procedure

Precautions:
Keep dry prior to insertion into the body.
Replace catheter if it comes into contact with fluid prior to use.
Handle catheter only with sterile gloves. Minimize contact with the coated balloon.

1. Select the appropriate size SurVeil DCB to provide full vessel wall apposition (balloon to artery ratio of 1.1:1). Treatment with the SurVeil DCB Catheter must cover the entire lesion or area treated by the pre-dilatation balloon catheter, whichever is longer, plus a minimum of 5 mm proximally and 5 mm distally beyond the margins.
2. Prepare the necessary accessories to perform the procedure.

Remove air from the SurVeil DCB using the following steps:

1. Prepare a syringe with 2-3 mL mixture of inflation solution (50% contrast / 50% sterile saline).
2. With the syringe tip down, apply negative pressure to the balloon to purge the air from the device. Hold for ≥ 15 seconds. Gently release the vacuum and remove from balloon inflation port.
3. Repeat steps 1 and 2 until all air is expelled. If bubbles persist, do not use device.
4. Disconnect the syringe.

Warning: Use only the recommended balloon inflation solution (50% contrast / 50 % sterile saline).
Warning: Do not use device if air does not aspirate properly.

11.6 Inflation Device Connection to SurVeil DCB

1. Remove the balloon from the protective dispenser hoop.
2. Attach inflation device filled with inflation solution (50% contrast / 50% saline) to the balloon inflation port. Ensure there is a meniscus at the connecting end prior to making the connection.
3. Apply and maintain negative pressure on the SurVeil DCB.
4. To remove the protective sheath, gently grasp the midpoint of the balloon sheath, and pull it off the distal end of the SurVeil DCB.
5. *Precaution: If it is difficult to remove the balloon sheath, use a new SurVeil DCB.*
6. With the balloon tip down and the catheter in a vertical position, flush the guidewire lumen with heparinized saline through the Luer Lock.

11.7 Load catheter onto guidewire and advance

With a 0.035” guidewire and the introducer in place, perform the following steps to prepare the catheter guidewire assembly:

1. Load the distal tip of the drug coated balloon catheter onto the proximal end of the guidewire. NOTE: If possible, avoid contact with the coated balloon during guidewire loading and catheter advancement. If it is necessary to grasp the balloon, use dry gauze with gentle pressure.
2. With the balloon fully deflated and under negative pressure, advance the balloon catheter to the proximal portion of the rotating hemostatic valve and stop. Open the valve to allow the SurVeil DCB to pass through the valve with minimal surface contact on the coating. NOTE: step not required if using a sheath without rotating hemostatic valve.
3. Once the SurVeil DCB has passed through the fully opened rotating hemostatic valve, stop advancing the catheter to close the rotating hemostatic valve. Close the valve around the shaft of the SurVeil DCB. Do not over-tighten the hemostatic valve around the SurVeil DCB as lumen constriction may occur, affecting inflation/deflation of the balloon. NOTE: step not required if using a Sheath without rotating hemostatic valve.
4. Advance the SurVeil DCB into the vasculature in small increments until the stenosis is centered within the radiopaque marker bands. Radiopaque marker bands delineate the treatment area of the coated balloon. Position the SurVeil DCB relative to the lesion, ensuring coverage of at least 5 mm proximally and distally beyond the margins of the pre-dilatated lesion. See Figure 5.

Precaution: The position of the SurVeil DCB may only be changed with the guidewire in place.

Precaution: Do not advance the SurVeil DCB if resistance is met.

Figure 5. Centering of the stenosis within the SurVeil DCB radiopaque marker bands

5. When the radiopaque marker bands are in the proper position (See Figure 5), inflate the balloon as soon as possible, using an inflation device with manometer. Inflate the balloon to a pressure that yields a balloon to artery ratio of 1.1:1. Approximate balloon inflated diameters are provided in the compliance chart on the package label. Inflate the balloon for a minimum of 120 seconds.

Warnings: Do not exceed the rated burst pressure (RBP) recommended on the device labeling for this device. Balloon rupture may occur if the RBP is exceeded. To prevent over-pressurization, use a manometer to monitor pressure.

Precaution: Do not inflate the balloon outside the body or prior to reaching the target segment as it may disrupt the drug coating.

11.8 Deflate and remove balloon

Warning: Completely deflate the balloon and maintain negative pressure before withdrawing it from the dilated area.

1. Apply negative pressure to fully deflate the SurVeil DCB.
2. Confirm that the balloon is fully deflated under fluoroscopy.
3. While maintaining negative pressure, withdraw the deflated SurVeil DCB from the introducer and through the rotating hemostatic valve.
4. Remove and discard.

If multiple SurVeil DCBs are required to treat a lesion, the balloons must overlap by at least 1 cm. The additional SurVeil DCB should be minimally sized and angiographically positioned to ensure coverage of at least 5 mm proximally and distally beyond the margins of the pre-dilatation lesion. Do not exceed the maximum usage requirements included in the Warnings (Section 4) above.

5. Confirm dilatation of the lesion using angiography.

NOTE: If additional dilatation is required, use a standard percutaneous transluminal angioplasty balloon catheter. Whenever possible, the SurVeil DCB should be the final treatment; however, post-dilatation is allowed.

6. When complete, remove all equipment from the body and close access site per standard clinical practice.

11.9 Disposal

After use, the SurVeil DCB may be a potential biohazard. Handle and dispose the SurVeil DCB in accordance with acceptable medical practices and applicable local, state, and federal laws and regulations.

12 DISCLAIMER OF WARRANTY

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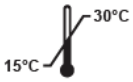
Graphical Symbols for Medical Device Labelling

Rx ONLY	CAUTION: Federal law restricts this device to sale by or on the order of a licensed physician	IP	Inflation pressure
	Consult instructions for use or electronic instructions for use	NP	Nominal pressure
	Do not use if packaging is damaged	RBP	Rated burst pressure
	Keep dry	RBP	Do not exceed rated burst pressure
LOT	Lot number	BALLOON ⌀	Balloon diameter
REF	Reference number		Contents
	Use-by date		Do not re-sterilize
	Do not reuse	STERILE R	Sterilized using irradiation
	Date of manufacture		Manufacturer
OTW	Over the wire		Non-pyrogenic
DCB	Drug-Coated Balloon		Temperature limit (15°C – 30°C)
REC SHEATH	Minimum introducer sheath	UDI	Unique Device Identifier
REC GW	Maximum guidewire diameter		Distributed by