AGENT™
MONORAIL™

Paclitaxel-Coated Balloon Catheter

Directions for Use

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

REUSE WARNING STATEMENT
For single use only. Do not reuse, reprocess or resterilize. Reuse, reprocessing or resterilization may compromise the structural integrity of the device and/or lead to device failure which, in turn, may result in patient injury, illness or death. Reuse, reprocessing or resterilization may also 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) from one patient to another. Contamination of the device may lead to injury, illness or death of the patient.

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

Do not use if sterile barrier is damaged. If damage is found, call your Boston Scientific representative.

DEVICE DESCRIPTION
The AGENT Paclitaxel-Coated Balloon Catheter (AGENT Drug-Coated Balloon) is a monorail, semi-compliant percutaneous coronary intervention (PCI) catheter; the balloon portion of the device is coated with TransPax, a formulation of a drug (paclitaxel) and excipient [acetyl tributyl citrate (ATBC)].

The AGENT Drug-Coated Balloon (DCB) is designed to inhibit restenosis by delivering drug to diseased arterial tissue. The distal section of the catheter is dual lumen and coaxial. The outer lumen is used for inflation of the balloon to conform to the vessel wall, and the inner lumen permits the use of guidewires ≤ 0.014 in (0.36 mm) to facilitate advancement of the catheter. The proximal section of the catheter is a single-lumen, stainless steel hypotube with a single luer port hub for inflation/deflation of the balloon during drug delivery. The semi-compliant balloon is designed to provide an inflatable segment of known diameter and length at recommended pressures. A balloon protector is placed over the drug-coated balloon to maintain a low profile; a mandrel is placed into the inner lumen to protect the patency of the catheter during storage. The catheter tip is tapered to facilitate advancement of the catheter to the treatment area and through the stenosis. The shaft features the ZGlide hydrophilic coating, which is present from the guidewire port to just proximal to the balloon. The effective length of the catheter is 144 cm. Marks on the proximal portion of the catheter shaft indicate the exit of the balloon catheter tip out of the guide catheter (one mark at 90 cm and two marks at 100 cm). Two radiopaque marker bands, in conjunction with fluoroscopy, aid in positioning the AGENT Drug-Coated Balloon. An image of the AGENT Drug-Coated Balloon Catheter is provided in **Figure 1**.

A CLIPIT Hypotube Clip is also provided to aid in securing the catheter.

It is recommended the AGENT Drug-Coated Balloon Catheter is used in conjunction with guidewires that are ≤ 0.014 in (< 0.36 mm) and guide catheters that are ≥ 5 F (0.056 in / 1.42 mm) (reference **Table 1**).

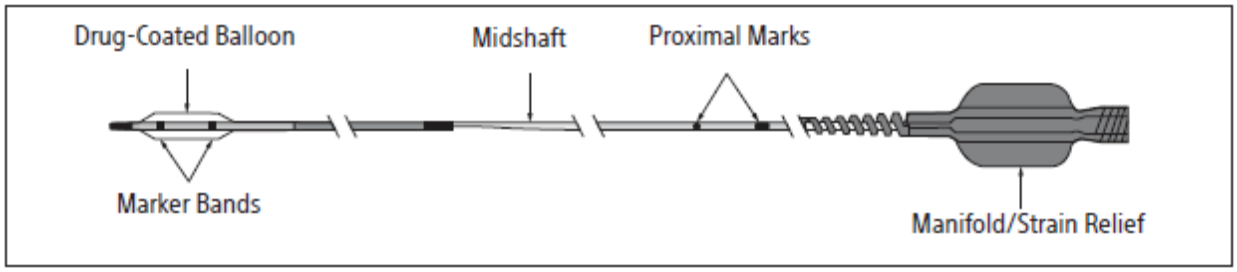

Figure 1: AGENT Drug-Coated Balloon Catheter

Table 1: Guidewire and Guide Catheter Compatibility

Balloon Diameter (All Lengths)	Recommended Guide Catheter	Guidewire Compatibility	Nominal Pressure	Rated Burst Pressure
2.00 mm to 3.00 mm	≥ 5F 1.42 mm)	≤ 0.014 in (0.036 mm)	6 ATM (88 psi)	14 ATM (206 psi)
3.50 mm and 4.00 mm	≥ 5F (1.42 mm)	≤ 0.014 in (0.036 mm)	6 ATM (88 psi)	12 ATM (176 psi)

Drug Component Description

The drug coating formulation for the AGENT Balloon Catheter consists of a drug substance (i.e., paclitaxel, the active pharmaceutical ingredient) and an excipient (i.e., acetyl tributyl citrate, the inactive ingredient). The dose density of paclitaxel is 2.0 µg per mm^2 of the balloon surface; the nominal drug content per balloon size is shown in **Table 2**.

Table 2: Nominal Drug Content Per Balloon Size

Diameter (mm)	Drug Dose by Balloon Length			
	12 mm	**15 mm**	**20 mm**	**30 mm**
2.00	165 µg	204 µg	272 µg	406 µg
2.25	177 µg	219 µg	291 µg	435 µg
2.50	196 µg	243 µg	322 µg	482 µg
2.75	216 µg	266 µg	354 µg	529 µg
3.00	235 µg	290 µg	386 µg	577 µg
3.50	274 µg	338 µg	449 µg	672 µg
4.00	312 µg	386 µg	513 µg	767 µg

Contents

Qty	Material
1	AGENT Drug-Coated Balloon Catheter
1	CLIPIT Hypotube Clip

Operating Principle

The AGENT Drug-Coated Balloon Catheter is a device/drug combination product consisting of a monorail, semi-compliant intracoronary balloon catheter with a drug coating [i.e., paclitaxel/acetyl tributyl citrate (PTx/ATBC)] on the balloon component. AGENT DCB provides mechanical expansion of a diseased vessel while transferring a pharmacological agent (i.e., paclitaxel) to inhibit neointimal proliferation of the vessel wall.

Materials

Drug Component Description

The AGENT Drug-Coated Balloon Catheter has a drug coating formulation consisting of paclitaxel (the active pharmaceutical ingredient), and an inactive citrate ester excipient (ATBC).

Paclitaxel

The active pharmaceutical ingredient in the balloon coating is paclitaxel. It is a white powder, isolated from a spectrum of Taxus (yew) species and hybrids. The dose of paclitaxel is 2.0 µg per mm^2 of balloon surface. The chemical name of paclitaxel is:
Benzenepropanoic acid, β - benzoylamino) α - hydroxy -, 6, 12b – bis (acetyloxy) - 12- (benzoyloxy) - 2a, 3, 4, 4a, 5, 6, 9, 10, 11, 12, 12a, 12b - dodecahydro - 4, 11 - dihydroxy-4a, 8, 13, 13 - tetramethyl - 5 - oxo - 7, 11 methano - 1H - cyclodeca [3, 4] benz [1, 2 -b] oxet - 9 - yl ester, [2aR2aα, 4β, 4aβ, 6β, 9α (αR*, βS*), 11α, 12α, 12aα, 12bα]].

Paclitaxel is a diterpenoid with a characteristic taxane skeleton of 20 carbon atoms, a molecular weight of 853.91 g/mol and a molecular formula of $C_{47}H_{51}NO_{14}$. It is highly lipophilic and insoluble in water, but freely soluble in polar solvents such as methanol, ethanol, chloroform, ethyl acetate, and dimethyl sulfoxide.

Acetyl Tributyl Citrate

The coating utilizes the inactive ingredient acetyl tributyl citrate (ATBC) as an excipient to facilitate the release and transfer of paclitaxel into the arterial wall. ATBC is a carboxylic acid ester with a molecular weight of 402.48 g/mol.

Non-Pyrogenic

This device meets pyrogen limit specifications.

User Information

Intended users of the device are interventional cardiologists, catheterization lab technicians, and nurses trained in angiography and percutaneous coronary intervention (PCI) procedures.

INTENDED USE / INDICATIONS FOR USE

The AGENT Paclitaxel-Coated Balloon Catheter is intended to be used after appropriate vessel preparation in adult patients undergoing percutaneous coronary intervention (PCI) in coronary arteries 2.0 mm to 4.0 mm in diameter and lesions up to 26 mm in length for the purpose of improving myocardial perfusion when treating in-stent restenosis (ISR).

CONTRAINDICATION

Use of the AGENT Drug-Coated Balloon Catheter is contraindicated in the following:

- Use in the supra-aortic/cerebrovascular arteries.
- Unprotected native left main coronary artery disease.
- Coronary artery spasm in the absence of a significant stenosis.
- Patients with known hypersensitivity to paclitaxel (or structurally-related compounds).
- Patients who cannot receive recommended antiplatelet and/or anticoagulant therapy.
- Pregnant or breast-feeding women or women who are intending to become pregnant, or men intending to father children.

WARNINGS

- The drug-coated balloon catheter should only be used by physicians experienced in percutaneous coronary intervention.
- As for all PCI procedures, the need for on-site surgical backup should be considered per the 2023 SCAI Expert Consensus Statement on Percutaneous Coronary Interventions Without On-Site Surgical Backup.
- As for all PCI procedures, use in patients who are not acceptable candidates for open heart surgery requires careful consideration, including possible hemodynamic support during the procedure, as treatment of this patient population carries special risk.
- Use extreme caution and careful judgment in patients who have severe reaction to contrast agents that cannot be adequately pre-medicated.
- Use only the recommended balloon inflation medium (50:50 mixture of contrast medium and sterile saline solution). Never use air or any gaseous medium to inflate the balloon.
- When the balloon catheter is exposed to the vascular system, it should be manipulated using high-quality fluoroscopic observation.
- Do not advance or withdraw the catheter unless the drug-coated balloon is fully deflated under vacuum. If unusual resistance is felt during manipulation, determine the cause of the resistance before proceeding. If the source of resistance cannot be determined, it is recommended to extract the entire system (as a unit) with the guide catheter.
- If difficulty is experienced during drug-coated balloon treatment, do not continue. Deflate the device and remove the catheter.
- To reduce the potential for vessel damage, the inflated diameter and length of the balloon should approximate the diameter and length of the vessel just proximal and distal to the stenosis.
- Do not exceed the rated burst pressure indicated on the compliance chart. Use of an inflation device is recommended to assure accurate pressurization.
- If difficulty is experienced removing the device, other retrieval methods (additional wires, snares and/or forceps) may cause vessel trauma. Complications can include but are not limited to bleeding, hematoma, or pseudoaneurysm.
- The safety and effectiveness of using more than one AGENT DCB to treat a single lesion or multiple lesions/vessels per procedure has not been established. Preclinical studies suggest that use of multiple DCBs within a single coronary vessel may be associated with downstream perivascular inflammatory injury as a consequence of microvascular obstruction.

PRECAUTIONS

- Any use for procedures other than those indicated in these instructions is not recommended.
- Use the drug-coated balloon catheter prior to the “Use By” date specified on the package.
- The treatment site should be adequately prepared (intravascular imaging guidance recommended) to achieve the maximum lumen diameter prior to treatment with AGENT Drug-Coated Balloon.

  Note: Current US and European PCI guidelines recommend intravascular imaging (IVUS) to identify the mechanism of stent failure.[1, 2]
- Drug-coated balloon PCI should be used with caution during procedures involving calcified vessels due to the abrasive nature of these lesions.
- Significant stenosis (> 50 %) proximal to the treatment site must be pretreated to prevent abrasion and delamination of the balloon’s drug coating while crossing the lesion.
- Precautions to prevent or reduce thrombosis should be taken during any PCI procedure:
  - The patient should be treated with heparin or similar agent during the procedure.
  - Flush all products entering the vascular system with heparinized sterile isotonic saline or a similar solution prior to use.
- Carefully inspect the drug-coated balloon catheter prior to use to verify it has not been damaged during shipment or preparation; confirm that its size, shape, and condition are suitable for the procedure.

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[1] 2023 SCAI Expert Consensus Statement

[2] Moussa ID, Klein LW, Shah B, et al. Consideration of a New Definition of Clinically Relevant Myocardial Infarction After Coronary Revascularization: An Expert Consensus Document From the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol*. 2013;62(17):1563-1570.

Note: After removing the balloon protector, a white powdery substance may be observed inside the balloon protector and will not impact the delivered drug dose.

- If unusual resistance is felt during removal of the balloon protector or mandrel, do not use the AGENT device and replace with another.
- Do not expose the drug-coated balloon catheter to organic solvents such as alcohol or detergents.
- When loading or exchanging the balloon catheter, it is recommended to thoroughly wipe the guidewire with heparinized saline to improve catheter movement on the guidewire.
- Do not touch, wipe, bend, or squeeze the drug-coated balloon, or allow it to come into contact with any liquids prior to insertion as damage to the device's drug coating or premature release of the drug may occur.
- If using a Tuohy-Borst type adapter, take care to not over-tighten the hemostatic valve around the catheter shaft as lumen constriction may occur, affecting inflation/deflation or damaging the device's drug coating.
- Never advance the drug-coated balloon catheter without the guidewire extending from the tip. Do not use the AGENT DCB if the lesion is unable to be crossed with a guidewire.
- The AGENT DCB is indicated for lesions up to 26 mm using one balloon. The safety and effectiveness of treating lesions longer than 26 mm has not been established. When clinically warranted, observe the following precautions to prevent local drug overdosing:
    - If treating a long lesion (longer than the maximum balloon length available), each individual segment should be treated only once with a drug-coated balloon. Treat each segment with a new balloon and try to minimize overlapping the treated segments.
    - Do not use a second drug-coated balloon at the same treatment site.
- The AGENT DCB was not studied clinically with use of bail out stenting, including drug-eluting stents (DES). Implanting a drug-eluting stent at the same treatment site may have added risks, including overdosage or interaction between the active agents.
- Published literature has reported paclitaxel caused cell aneuploidy at tissue concentrations similar to tissue concentrations recorded after treatment with an AGENT Drug-Coated Balloon in preclinical studies. The aneugenic effect is due to paclitaxel's pharmacodynamic action of interfering with microtubule disassembly, which is also the basis for the pharmacodynamic action preventing restenosis in vascular tissue following treatment with an AGENT Drug-Coated Balloon. The relevance of both this observation and the aneugenic mechanism of genotoxicity for human carcinogenicity is currently not known.
- The AGENT Drug-Coated Balloon has not been tested in pregnant women or in men intending to father children; effects on the developing fetus have not been studied. The risks and reproductive effects of paclitaxel administered through the coronary vasculature remain unknown. The AGENT Drug-Coated Balloon is contraindicated for use in women who are pregnant or attempting to conceive, or men intending to father children. It is not known whether paclitaxel is distributed in human milk. In lactating rats given paclitaxel, milk concentrations appeared to be higher than maternal plasma levels and declined in parallel with the maternal levels.
- Possible interactions between paclitaxel and concomitantly administered medications have not been formally investigated. Drug interactions of systemic chemotherapeutic levels of paclitaxel with possible concomitant medications are outlined in the labeling for finished pharmaceuticals containing paclitaxel, such as TAXOL.
- The optimal duration of dual anti-platelet therapy (DAPT) post PCI for ISR is currently unknown. Published expert consensus opinion[3] has suggested that DAPT should be used for a minimum of one month post ISR PCI. While the AGENT DCB IDE required that enrolled subjects receive a minimum of 1-month of DAPT followed by antiplatelet monotherapy for the duration of the study, more than 70 % of enrolled patients remained on DAPT for at least 1 year. In conjunction with this information, operators should use clinical judgment in deciding on the duration of DAPT following use of AGENT DCB.

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

[3] 2023 SCAI Expert Consensus Statement.

gene mutation assay; however, it has been shown to be clastogenic (causing chromosome aberrations) in vitro in human cells as well as in vivo in the mouse micronucleus assay. This effect is likely due to the mechanism of action of paclitaxel wherein it interferes with normal microtubule organization during cell division. Reproductive toxicity of paclitaxel has been evaluated in rats and rabbits. Administration of paclitaxel prior to and during mating produced impairment of fertility in male and female rats at doses ≥ 1 mg/kg/day and increased embryo- and fetotoxicity. Administration of paclitaxel during the period of organogenesis to rabbits at doses of 3 mg/kg/day caused embryo- and fetotoxicity. Maternal toxicity was also observed at this dose. No teratogenic effects were observed at 1 mg/kg/day. For comparison, the worst-case dose of paclitaxel delivered by the AGENT DCB (assuming maximum size and number of balloons used in a lesion) is 767 µg, which is approximately 78 times and 235 times less than the dose that saw effects in rats and rabbits, respectively, when normalizing to body weight.

ADVERSE EVENTS

Potential adverse events which may be associated with the use of a drug-coated balloon (DCB) or DCB procedure include, but are not limited to, the following:

- Additional, possibly surgical, intervention
- Allergy (drug coating and its components, device, medications, contrast)
- Arrhythmia including conduction system disorder
- Bleeding (including hemorrhage or hematoma possibly requiring transfusion or additional intervention)
- Cerebrovascular accident (stroke)/transient ischemic attack (TIA)
- Death
- Embolism (tissue, plaque, thrombus, device, drug coating)
- Fever/inflammation
- Hemodynamic instability
- Hypotension/hypertension (shock)
- Kidney injury/failure
- Myocardial ischemia/infarction
- Organ insufficiency/failure (heart, liver, lungs
- Pain (anginal, non-anginal)
- Pericardial effusion/cardiac tamponade
- Radiation injury
- Sepsis/infection
- Slow flow/no reflow
- Vessel injury (spasm, dissection, perforation, rupture, arteriovenous fistula, aneurysm)
- Vessel occlusion (abrupt closure, slow flow/no reflow, thrombosis, restenosis)

Potential adverse events not captured above that have been associated with administration of paclitaxel at systemic doses, include, but are not limited to, the following:

- Abnormal liver enzymes
- Allergic/immunologic reaction to drug (paclitaxel or structurally-related compounds)
- Alopecia
- Anemia
- Blood product transfusion
- Gastrointestinal symptoms
- Hematologic dyscrasia (including leukopenia, neutropenia, thrombocytopenia)
- Hepatic enzyme changes
- Histologic changes in vessel wall, including inflammation, cellular damage or necrosis
- Myalgia/arthralgia
- Peripheral neuropathy

CLINICAL STUDIES

AGENT IDE Study

Primary Objective:
The primary objective of the AGENT IDE study was to assess the safety and effectiveness of the AGENT Drug-Coated Balloon (DCB) compared to plain old balloon angioplasty (POBA) in patients with in-stent restenosis (ISR) of a previously treated lesion of up to 26 mm in length (by visual estimate) in a native coronary artery 2.0 mm to 4.0 mm in diameter.

Study Design:

The AGENT IDE clinical study is a prospective, multicenter, 2:1 randomized (AGENT DCB to POBA), controlled, single-blind, superiority trial to assess the safety and effectiveness of the AGENT DCB in patients with ISR. Patients ≥ 18 years of age with ISR of a previously treated lesion with visually estimated length < 26 mm and reference vessel diameter > 2.00 mm to ≤ 4.00 mm, and % diameter stenosis (DS) > 50 % and < 100 % (symptomatic) or % DS > 70 % and < 100 % (asymptomatic) were eligible for enrollment. Successful target lesion pre-treatment was required. Patients were randomized 2:1 to AGENT DCB or POBA after they met trial selection criteria, had signed the informed consent, and the target lesion was successfully pre-dilated.

During the index procedure, up to 2 native coronary artery lesions in 2 major epicardial vessels could be treated. Patients could have 1 target lesion, or 1 target lesion and 1 non-target lesion (in non-target vessel) treated. For patients who were not taking aspirin and/or a $P2Y_{12}$ inhibitor at the time of the index procedure, a loading dose of these medications was recommended. Dual anti-platelet therapy (DAPT) with a $P2Y_{12}$ inhibitor for a minimum of 1 month was required post-procedure. Antiplatelet monotherapy was to be continued for the duration of the study.

The primary endpoint was the 1-year rate of target lesion failure (TLF) defined as any ischemia-driven revascularization of the target lesion (TLR), myocardial infarction (MI; Q-wave and non-Q-wave) related to the target vessel, or cardiac death. Peri-procedural MI (within 48 hours of the procedure) was defined per the SCAI definition[4] and spontaneous MI (more than 48 hours after the procedure) was defined per the 4th Universal definition.[5]

AGENT IDE used an adaptive group-sequential design[6] with an initial planned enrollment of 480 patients and one formal interim analysis on the 1-year data after randomization of the first 90 % of patients, with the expectation that the first 40 % of randomized patients would have 1-year follow up at that time. The interim analysis was prespecified to be performed by the Data Monitoring Committee (DMC) for potential sample size re-estimation of up to 600 patients. Due to rapid enrollment in the trial, no patients had completed 1-year follow-up for the interim analysis at the time of the planned interim analysis, and therefore, the DMC recommended to continue enrollment to the maximum of 600 patients. To determine final sample size for the primary endpoint analysis, it was agreed upon with the US FDA that the DMC perform an interim analysis on the first 40 % patients (n=192) with 1-year data when those data were available using the prespecified adaptive design strategy. Based on this interim analysis, the recommendation was to evaluate the primary endpoint on the first 480 patients, which was consistent with the initial planned sample for the trial.

The AGENT IDE study enrolled 600 patients. Of the 600 patients, 406 AGENT and 194 POBA, were randomized and enrolled at 40 sites in the United States. Follow-up included clinical assessments at hospital discharge, 30 days, 6 months, 1 year, and then annually for 5 years post procedure. Patients who were enrolled but who did not receive treatment were followed through 12 months only.

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[4] Moussa ID, Klein LW, Shah B, et al. Consideration of a New Definition of Clinically Relevant Myocardial Infarction After Coronary Revascularization: An Expert Consensus Document From the Society for Cardiovascular Angiography and Interventions (SCAI). *J Am Coll Cardiol*. 2013;62(17):1563-1570.

[5] Thygesen Kristian, Alpert Joseph S., Jaffe Allan S., et al. Fourth Universal Definition of Myocardial Infarction (2018). *J Am Coll Cardiol*. 2018;72(18):2231-2264.

[6] Mehta CR, Pocock SJ. Adaptive increase in sample size when interim results are promising: A practical guide with examples. *Stat Med*. 2011;30(28):3267-3284.

The primary endpoint of 1-year TLF was analyzed based on the primary endpoint cohort (N=480). The primary endpoint analysis was also performed on the total enrollment cohort (N=600). Results for both are presented below. All other data is based on the total enrollment cohort (N=600).

The following data summarize the results of the AGENT IDE study through 1 year (N=600).

Demographics

Table 3 presents demographic and baseline clinical characteristics for the ITT analysis set. AGENT and POBA treatment groups were well-balanced with no significant differences in baseline characteristics. The mean age of patients was 68.3 years. 26.2 % of patients were female and 75.3 % were white. Diabetes was present in 50.7 % of patients.

Table 3: Baseline Demographic and Clinical Characteristics, ITT (N=600)

Baseline Characteristic	POBA N=194	AGENT DCB N=406	P-value
Demographics			
Age at time of consent (years)	67.90 ± 9.68 (194)	68.42 ± 9.79 (406)	0.54
Female	27.3 % (53/194)	25.6 % (104/406)	0.66
Male	72.7 % (141/194)	74.4 % (302/406)	0.66
Race†			
American Indian or Alaska Native	0.5 % (1/194)	0.0 % (0/406)	0.32
Asian	3.1 % (6/194)	2.2 % (9/406)	0.58
Black or African American	5.2 % (10/194)	7.9 % (32/406)	0.22
White	76.3 % (148/194)	74.9 % (304/406)	0.71
Native Hawaiian or other Pacific Islander	0.5 % (1/194)	0.2 % (1/406)	0.54
Other	1.5 % (3/194)	3.9 % (16/406)	0.12
Not Disclosed	9.3 % (18/194)	5.7 % (23/406)	0.10
Ethnicity			
Hispanic or Latino	4.6 % (9/194)	6.4 % (26/406)	0.39
Physical Assessment			
Height (cm)	171.98 ± 9.83 (191)	172.12 ± 10.55 (396)	0.88
Weight (kg)	89.65 ± 21.67 (193)	89.07 ± 18.48 (404)	0.74
Body mass index‡ (kg/m^2)	30.10 ± 5.85 (191)	30.01 ± 5.53 (396)	0.86
Medical History			
Smoking, Ever	57.7 % (112/194)	57.6% (234/406)	0.98
Current	9.8 % (19/194)	10.3% (42/406)	0.83
Previous	47.9 % (93/194)	47.3% (192/406)	0.88
Smoking, Unknown	0.0 % (0/194)	1.7% (7/406)	0.10
Current Diabetes Mellitus	50.0 % (97/194)	51.0% (206/404)	0.82
Current Method of Treatment			
Diet	3.1 % (6/194)	5.4 % (22/404)	0.20
Medically Treated	46.4 % (90/194)	44.3 % (179/404)	0.63
Oral agent	37.6 % (73/194)	34.4 % (139/404)	0.44
Insulin or other injectables	25.3 % (49/194)	23.0 % (93/404)	0.55
Unknown	0.5 % (1/194)	1.2 % (5/404)	0.67
Hyperlipidemia	94.8 % (184/194)	94.6 % (382/404)	0.88
Hypertension	95.9 % (186/194)	94.6 % (383/405)	0.49
History of bleeding disorder	2.6 % (5/193)	2.3 % (9/399)	0.78
History of PVD	16.1 % (31/192)	19.5 % (78/401)	0.33
History of chronic obstructive pulmonary disease	10.3 % (20/194)	9.7 % (39/403)	0.81
Neurological History			
History of TIA	5.2 % (10/194)	6.7 % (27/401)	0.45
History of CVA	7.2 % (14/194)	9.2 % (37/401)	0.41
History of TIA or CVA	9.8 % (19/194)	14.2 % (57/402)	0.13

Baseline Characteristic	POBA N=194	AGENT DCB N=406	P-value
Renal History			
History of renal disease	16.6 % (32/193)	18.4 % (74/402)	0.59
COVID-19 History			
Does the subject have a history of COVID-19 infection?	13.3 % (23/173)	13.0 % (49/376)	0.93
Has the subject been vaccinated for COVID-19?	84.7 % (138/163)	87.2 % (287/329)	0.43

Numbers are presented as % (count/sample size) or mean ± standard deviation (n).
P-values are 2-sided and from Student's t Test for continuous variables and the Chi-square or Fisher's Exact (*) Test for discrete variables. The p-values have not been adjusted for multiplicity.
†A subject may be identified in multiple ethnicity and race categories.
‡The body mass index is the weight in kilograms divided by the square of the height in meters.
Abbreviation: CVA=cerebrovascular accident; ITT=intent-to-treat; NA=not applicable; PVD=peripheral vascular disease; TIA=transient ischemic attack; Undef=undefined.

Cardiac history is presented in **Table 4**. AGENT and POBA treatment groups were well-balanced with no significant differences in baseline characteristics. 30.1 % of patients had a history of prior coronary artery bypass grafting. History of multivessel disease and left main disease was present in 79.0 % and 22.0 % of patients, respectively.

Table 4: Cardiac History, ITT (N=600)

Cardiac History	POBA N=194	AGENT DCB N=406	P-value
Family History of CAD	99.5 % (193/194)	99.8 % (405/406)	0.54
History of MI	50.0 % (95/190)	49.7 % (198/398)	0.95
History of CABG	28.6 % (55/192)	30.8 % (124/403)	0.60
History of CHF	21.4 % (41/192)	22.9 % (92/401)	0.66
NYHA Classification			0.56
I	3.6 % (7/192)	2.0 % (8/401)	0.27
II	7.3 % (14/192)	8.0 % (32/401)	0.77
III	5.2 % (10/192)	4.7 % (19/401)	0.80
IV	0.0 % (0/192)	0.0 % (0/401)	Undef
Unknown	5.2 % (10/192)	8.2 % (33/401)	0.18
History of Arrhythmia	18.2 % (35/192)	21.9 % (88/401)	0.30
Indication for Procedure			
Recent MI +	6.2 % (12/194)	5.2 % (21/406)	0.61
Unstable angina	31.4 % (61/194)	31.5 % (128/406)	0.98
Stable angina	51.5 % (100/194)	55.4 % (225/406)	0.37
Silent ischemia	2.6 % (5/194)	1.7 % (7/406)	0.54
Other indication	8.2 % (16/194)	6.2 % (25/406)	0.34
LVEF Measurement (%)	54.23 ± 9.89 (189)	54.05 ± 10.56 (393)	0.84
History of Multivessel Disease	78.4 % (149/190)	79.3 % (317/400)	0.82
History of Left Main Disease	20.7 % (39/188)	22.6 % (89/394)	0.62

Numbers are presented as % (count/sample size) or mean ± standard deviation (n).
P-Values are two-sided from Fisher's exact test; p-values without are from the Chi-square test. The p-values have not been adjusted for multiplicity.
The Mantel-Haenszel (MH) tests use non-missing data and exclude the 'Unknown' category. For NYHA classification, the MH test is performed on all subjects with CHF. For CCS classification, the MH test is performed on all subjects with stable angina. For Braunwald classification, the MH test is performed on all subjects with unstable angina.
Questions reported in hierarchical order.
+ Recent MI defined as MIs that occurred within 2 weeks prior to the index procedure. Patients who had a STEMI 72 hours or less prior to the procedure were excluded from the study.
Abbreviation: CABG=coronary angiography bypass graft; CAD=coronary artery disease; CCS=Canadian Cardiovascular Society; CHF=congestive heart failure; ITT=intent-to-treat; LVEF=left ventricular ejection fraction; NA=not applicable; NYHA=New York Heart Association; MI=myocardial infarction; Undef=undefined.

Baseline Lesion Characteristics

Table 5 presents baseline lesion characteristics as determined by the core laboratory quantitative coronary angiography (QCA). The presence of multiple-layer in-stent restenosis, as reported by the site, was similar in both arms (AGENT 43.3% versus POBA 42.3%). By QCA, mean reference vessel diameter (2.7 ± 0.5 mm in both arms) and lesion length were comparable (AGENT 12.8 ± 6.3 mm vs. POBA 11.8 ± 6.6 mm).

Table 5: Baseline Lesion Characteristics as Determined by the Angiographic Core Laboratory, ITT (N=600)

Lesion Characteristic	POBA N=194 Lesions, N=194 Subjects	AGENT DCB N=407 Lesions, N=406 Subjects	P-value
Single Stent Layer†	57.7 % (112/194)	56.7 % (230/406)	0.80
Multiple Stent Layer†	42.3 % (82/194)	43.3 % (176/406)	0.80
Target Lesion Vessel			
LAD	35.6 % (69/194)	34.7 % (141/406)	0.84
LCx	24.2 % (47/194)	24.1 % (98/406)	0.98
RCA	35.6 % (69/194)	38.4 % (156/406)	0.49
LMCA	4.6 % (9/194)	2.7 % (11/406)	0.22
Lesion Location			
Proximal	32.0 % (62/194)	31.5 % (128/406)	0.92
Mid	40.2 % (78/194)	44.1 % (179/406)	0.37
Distal	12.4 % (24/194)	11.1 % (45/406)	0.64
Ostial	15.5 % (30/194)	13.3 % (54/406)	0.48
In-Lesion MLD (mm)	0.92 ± 0.40 (191)	0.95 ± 0.36 (405)	0.35
In-Lesion Mean Lumen Diameter (mm)	2.27 ± 0.58 (189)	2.31 ± 0.50 (399)	0.39
In-Lesion % Diameter Stenosis (mm)	66.41 ± 12.76 (191)	64.98 ± 12.05 (405)	0.19
Mehran ISR Pattern			
0	0.0 % (0/189)	0.0 % (0/403)	Undef
1A (articulation)	0.0 % (0/189)	0.0 % (0/403)	Undef
1B (margin)	1.1 % (2/189)	1.0 % (4/403)	1.00
1C (focal)	44.4 % (84/189)	36.7 % (148/403)	0.07
1D (multifocal)	1.1 % (2/189)	0.7 % (3/403)	0.66
2 (intrastent)	47.1 % (89/189)	57.1 % (230/403)	0.02
3 (proliferative)	4.8 % (9/189)	4.0 % (16/403)	0.66
4 (total occlusion)	1.6 % (3/189)	0.5 % (2/403)	0.33
Tortuosity, Any	0.0 % (0/192)	0.7 % (3/405)	0.55
Moderate	0.0 % (0/192)	0. 7% (3/405)	0.55
Severe	0.0 % (0/192)	0.0 % (0/405)	Undef
Calcification, Any	12.5 % (13/104)	12.6 % (28/222)	0.98
Moderate	2.9 % (3/104)	5.0 % (11/222)	0.56
Severe	9.6 % (10/104)	7.7 % (17/222)	0.55
Ulceration	1.5 % (3/194)	0.0 % (0/406)	0.03
Aneurysm	0.5 % (1/194)	0.0 % (0/406)	0.32
Pre-Procedure TIMI Flow			
0	3.1 % (6/192)	2.0 % (8/405)	0.39
1	1.6 % (3/192)	0.5 % (2/405)	0.33
2	4.2 % (8/192)	5.2 % (21/405)	0.59
3	91.1 % (175/192)	92.3 % (374/405)	0.61
Lesion Preparation (Pretreatment) †			
Target lesion successfully prepared	100 % (194/194)	99.5 % (405/407)	1.00

Numbers are presented as % (count/sample size) or mean ± standard deviation (n).
†Site-reported values.

Lesion Characteristic	POBA N=194 Lesions, N=194 Subjects	AGENT DCB N=407 Lesions, N=406 Subjects	P-value
Note: P-values are 2-sided and from Student's t Test for continuous variables and the Chi-square or Fisher's Exact *) Test for discrete variables. The p-values have not been adjusted for multiplicity. Abbreviations: ITT=intent-to-treat, ACC/AHA=American College of Cardiology/American Heart Association; MLD=minimum lumen diameter; RVD=reference vessel diameter; TIMI= Thrombolysis In Myocardial Infarction; LAD=left anterior descending; LCx=left circumfex; LMCA=left main coronary artery; NA=not applicable; RCA=right coronary artery; Undef=undefined.			

Procedural Characteristics

Table 6 presents procedural characteristics. The AGENT and POBA treatment groups were well-balanced with no significant differences in procedural characteristics. Mean procedure time was 55.2 minutes, 87.2 % of patients had only the target lesion treated, and 12.8 % of patients had both target plus one non-target lesion treated. Only one study device was allowed for the AGENT DCB arm, hence the slight difference in number of study devices used (3.6% of subjects in the POBA arm had 2 study devices used). The use of cutting balloon was similar in lesions treated with AGENT DCB as compared to lesions treated with POBA (25.1 % vs. 23.7 %, respectively). During the procedure, intravascular imaging was performed in approximately 74 % of patients.

Table 6: Procedural Characteristics, ITT (N=600)

Measure		POBA N=194 Lesions, N=194 Subjects	AGENT DCB N=407 Lesions, N=406 Subjects	P-value
Urgency of Intervention				
Elective		90.2 % (175/194)	89.7 % (364/406)	0.83
Urgent / Emergent		9.8 % (19/194)	10.3 % (42/406)	0.83
Procedure Time (min)		53.15 ± 27.06 (193)	56.19 ± 29.81 (402)	0.23
Target Lesions Treated by Subject		1.00 ± 0.00 (194)	1.00 ± 0.05 (406)	0.49
1 Target Lesion Treated		100 % (194/194)	99.8 % (405/406)	1.00
2 Target Lesions Treated		0.0 % (0/194)	0.2 % (1/406)†	1.00
Study Device Usage by Subject				
Target Lesion #1	0 study device	0.0 % (0/194)	0.2 % (1/406)‡	1.00
	1 study device	95.4 % (185/194)	99.8 % (405/406)	0.0002
	2 study devices	3.6 % (7/194)	0.0 % (0/406)	0.0003
	3 study devices	1.0 % (2/194)	0.0 % (0/406)	0.10
Target Lesion #2	1 study device	Undef (0/0)	100 % (1/1)†	Undef
Subjects with Only Target Lesion Treated		86.6 % (168/194)	87.4 % (355/406)	0.77
Subjects with Both Target & Non-Target Lesion Treated		13.4 % (26/194)	12.6 % (51/406)	0.77
Cutting Balloon Use		23.7 % (46/194)	25.1 % (102/407)	0.72
Intravascular Imaging Used During Procedure		76.8 % (149/194)	72.4 % (294/406)	0.25
Post-Procedure				
Hospital Length of Stay (days)		0.72 ± 1.75 (194)	0.59 ± 0.93 (406)	0.24

Numbers are presented as % (count/sample size) or mean ± standard deviation (n).
Note: P-values are two-sided and from Student's t Test for continuous variables and the Chi-square or Fisher's Exact (*) Test for discrete variables. The p-values have not been adjusted for multiplicity.
†One patient in the DCB arm had two target lesions treated with DCB that was counted as a protocol deviation.
‡Study balloon rupture in the DCB arm causing perforation. This was counted as a device deficiency.

Use of DAPT (aspirin plus a $P2Y_{12}$ inhibitor) pre-procedure, at hospital discharge, 30-day, 6-month, and 1-year follow-up time points is shown in **Table 7**. The percentage of subjects on DAPT was similar between the two treatment groups at each time point.

Table 7: Antiplatelet Medication Usage Through 1-Year, ITT (N=600)

Medication	POBA N=194	AGENT DCB N=406	P-value
Aspirin			
Prior regimen or loading dose	86.6 % (168/194)	85.7 % (348/406)	0.77
Discharge	95.4 % (185/194)	96.1 % (390/406)	0.69
30 Days	91.6 % (174/190)	92.0 % (368/400)	0.86
6 Months	88.4 % (168/190)	89.3 % (349/391)	0.76
12 Months	86.4 % (152/176)	86.9 % (324/373)	0.87
Clopidogrel			
Prior regimen or loading dose	54.6 % (106/194)	53.7 % (218/406)	0.83
Discharge	66.0 % (128/194)	66.3 % (269/406)	0.95
30 Days	65.3 % (124/190)	67.3 % (269/400)	0.63
6 Months	62.6 % (119/190)	64.5 % (252/391)	0.67
12 Months	59.7 % (105/176)	63.5 % (237/373)	0.38
Ticlopidine			
Prior regimen or loading dose	0.0 % (0/194)	0.0 % (0/406)	Undef
Discharge	0.0 % (0/194)	0.0 % (0/406)	Undef
30 Days	0.0 % (0/190)	0.0 % (0/400)	Undef
6 Months	0.0 % (0/190)	0.0 % (0/391)	Undef
12 Months	0.0 % (0/176)	0.0 % (0/373)	Undef
Prasugrel			
Prior regimen or loading dose	17.0 % (33/194)	16.5 % (67/406)	0.88
Discharge	18.6 % (36/194)	21.2 % (86/406)	0.45
30 Days	18.4 % (35/190)	20.8 % (83/400)	0.51
6 Months	16.8 % (32/190)	20.2 % (79/391)	0.33
12 Months	15.3 % (27/176)	17.7 % (66/373)	0.49
Ticagrelor			
Prior regimen or loading dose	14.9 % (29/194)	11.1 % (45/406)	0.18
Discharge	17.0 % (33/194)	12.6 % (51/406)	0.14
30 Days	15.8 % (30/190)	11.5 % (46/400)	0.15
6 Months	14.7 % (28/190)	11.3 % (44/391)	0.23
12 Months	15.9 % (28/176)	10.2 % (38/373)	0.05
Clopidogrel, Ticlopidine, Prasugrel or Ticagrelor			
Prior regimen or loading dose	85.1 % (165/194)	80.8 % (328/406)	0.20
Discharge	100 % (194/194)	99.5 % (404/406)	1.00
30 Days	98.4 % (187/190)	99.3 % (397/400)	0.39
6 Months	93.7 % (178/190)	95.9 % (375/391)	0.24
12 Months	90.3 % (159/176)	91.2 % (340/373)	0.76
Aspirin and one of Clopidogrel, Ticlopidine, Prasugrel or Ticagrelor			
Prior regimen or loading dose	77.8 % (151/194)	73.4 % (298/406)	0.24
Discharge	95.4 % (185/194)	95.8 % (389/406)	0.80
30 Days	90.5 % (172/190)	91.3 % (365/400)	0.77
6 Months	83.2 % (158/190)	85.7 % (335/391)	0.43
12 Months	77.8 % (137/176)	79.6 % (297/373)	0.63
Any of ASA, Clopidogrel, Ticlopidine, Prasugrel, Ticagrelor			
Prior regimen or loading dose	93.8 % (182/194)	93.1 % (378/406)	0.74
Discharge	100 % (194/194)	99.8 % (405/406)	1.00
30 Days	99.5 % (189/190)	100 % (400/400)	0.32
6 Months	98.9 % (188/190)	99.5 % (389/391)	0.60
12 Months	98.9 % (174/176)	98.4 % (367/373)	1.00

Numbers are % (count/sample size).
Note: P-values are 2-sided and from Student's t Test for continuous variables and the Chi-square or Fisher's Exact (*) Test for discrete variables. The p-values have not been adjusted for multiplicity.

Study Results

Primary Endpoint Analysis of the Primary Analysis Cohort (N=480): 12-Month TLF

Table 8 shows the primary endpoint of 1-year TLF for the primary endpoint analysis cohort (N=480). TLF to 1-year was observed in 18.2 % of patients treated with the AGENT DCB and 29.3 % of patients treated with POBA in the ITT population (difference= −11.1%; 97.5% UCB= −2.6%; P=0.0051 for superiority). A per-protocol analysis was also performed and the result was identical. The study primary endpoint was met. AGENT DCB was superior to POBA as the one-sided upper 97.5 % confidence bound for the difference in 1-year TLF was less than zero in the ITT population.

Table 8: Primary Endpoint Results, N=480

12-Month TLF	POBA (N=159)	AGENT DCB (N=321)	Difference [95 % CI]	One-sided 97.5 % UCB	One-sided *P*-value for superiority
ITT	29.3 % (44/150)	18.2 % (55/302)	-11.1 % [-19.6 %, -2.6 %]	-2.6 %	0.0051

Numbers are % (count/sample size).
P-value and CI are from z-test with unpooled variance for the difference of two proportions.
Events are based on CEC adjudication and MI is a composite event per SCAI definition for peri-procedural MI and the 4th Universal definition for spontaneous MI.
For the ITT analyses, all patients who signed informed consent and were enrolled in the study were included based on their randomized treatment assignment, regardless of whether the study or control device was used. The per-protocol analysis set included patients who received the assigned study or control device in the target coronary artery during the index procedure. While the ITT analysis was the primary analysis, the ITT analysis and per-protocol analyses were identical..
Abbreviations: ITT=intent-to-treat; TLF=target lesion failure (including any ischemia-driven revascularization of the target lesion, myocardial infarction [Q-wave and non–Q-wave] related to the target vessel, or any cardiac death).

Primary Endpoint Analysis of the Full Patient Cohort (N=600): 12-Month TLF

The primary endpoint was also analyzed in the total enrollment cohort (N=600). As shown in **Table 9**, the rate of 1-year TLF was 18.2 % in patients treated with AGENT DCB and 29.0 % in patients treated with POBA in the ITT population (difference=−10.8 %; 97.5 % UCB −3.3 %). These data demonstrate similar results of the AGENT DCB compared to POBA as the primary analysis cohort for the primary endpoint of 1-year TLF. A per-protocol analysis was also performed, and the result was identical.

Table 9: Primary Endpoint Results, N=600

12-Month TLF	POBA (N=194)	AGENT DCB (N=406)	Difference [95 % CI]	One-sided 97.5 % UCB
ITT	29.0 % (54/186)	18.2 % (71/390)	-10.8 % [-18.4%, -3.3 %]	-3.3 %

Numbers are % (count/sample size).
P-value and CI are from z-test with unpooled variance for the difference of two proportions.
Events are based on CEC adjudication and MI is a composite event per SCAI definition for peri-procedural MI and the 4th Universal definition for spontaneous MI.
For the ITT analyses, all patients who signed informed consent and were enrolled in the study were included based on their randomized treatment assignment, regardless of whether the study or control device was used. The per-protocol analysis set included patients who received the assigned study or control device in the target coronary artery during the index procedure. While the ITT analysis was the primary analysis, the ITT analysis and per-protocol analyses were identical.Abbreviations: ITT=intent-to-treat; TLF=target lesion failure (including any ischemia-driven revascularization of the target lesion, myocardial infarction [Q-wave and non–Q-wave] related to the target vessel, or any cardiac death).

Time-to-event event curves (Kaplan-Meier analysis) to 1 year for target lesion failure are shown below for the ITT analysis set in **Figure 2**. The estimated event rate was 17.9 % for AGENT and 28.6 % for POBA.

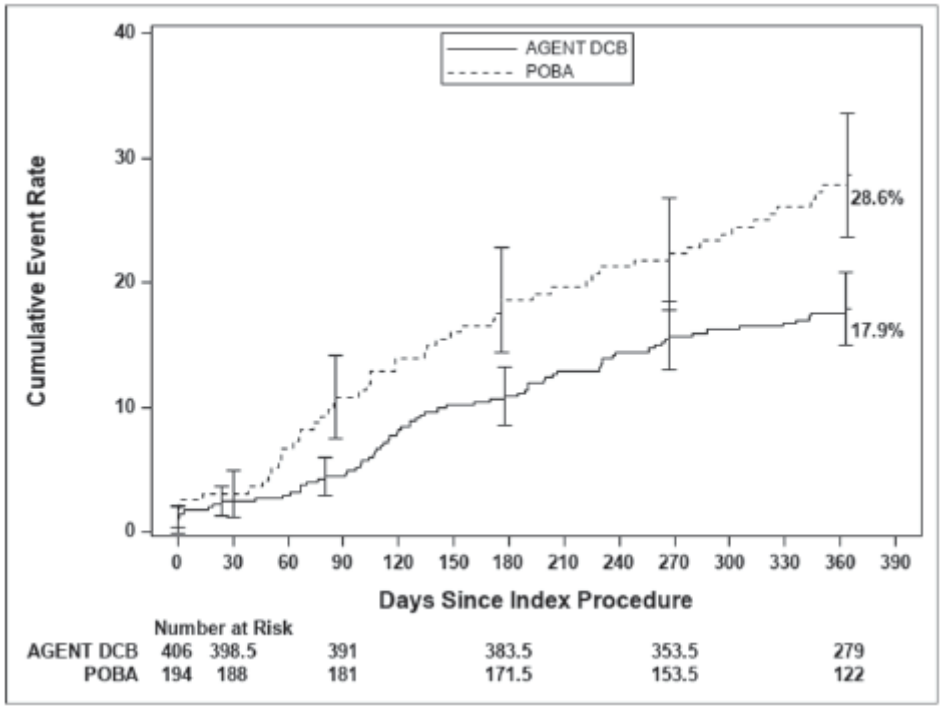

Figure 2: Kaplan-Meier Event Curve for TLF to 12 Months, N=600, Intent-to-Treat Analysis Set
Values are presented as cumulative event rate ± 1.5 standard error

Additional Clinical Endpoints through 12 Months

Additional clinical endpoints, including individual components of the primary endpoint, through 12 months are shown in **Table 10**.

- Target vessel related myocardial infarction (MI) occurred in 5.9 % of patients in the AGENT DCB arm versus 11.1% in the POBA arm.
- The rate of target lesion revascularization (TLR) was 13.0 % in AGENT DCB and 24.3 % in the POBA arm.
- The incidence of cardiac death was comparable (AGENT DCB 2.8 % versus POBA 1.6 %).
- None of the patients in the AGENT DCB arm experienced definite/probable ISR stent thrombosis compared to 6 patients in the POBA arm (0.0 % versus 3.2 %).

Table 10: Clinical Endpoints through 12 Months, ITT (N=600)

12-Month Clinical Endpoints	POBA (N=194)	AGENT DCB (N=406)
Total Evaluable Subjects	189	393
All Death, MI, TVR	31.7 % (60/189)	20.6 % (81/393)
All Death or MI	14.8 % (28/189)	10.4 % (41/393)
All Death	3.7 % (7/189)	4.1 % (16/393)
Cardiac Death	1.6 % (3/189)	2.8 % (11/393)
Non-Cardiac Death	2.1 % (4/189)	1.3 % (5/393)
MI	12.2 % (23/189)	7.4 % (29/393)
Related to TV	11.1 % (21/189)	5.9 % (23/393)
Related to TV-unknown	2.1 % (4/189)	2.8 % (11/393)
Not related to TV	1.1 % (2/189)	1.5 % (6/393)
Q-wave MI	0.5 % (1/189)	0.3 % (1/393)
Related to TV	0.5 % (1/189)	0.0 % (0/393)
Related to TV-unknown	0.0 % (0/189)	0.0 % (0/393)
Not related to TV	0.0 % (0/189)	0.3 % (1/393)
Non-Q-wave MI	11.6 % (22/189)	7.1 % (28/393)
Related to TV	10.6 % (20/189)	5.9 % (23/393)
Related to TV-unknown	2.1 % (4/189)	2.8 % (11/393)
Not related to TV	1.1 % (2/189)	1.3 % (5/393)
TVR, Overall	25.9 % (49/189)	14.2 % (56/393)
TVR, PCI	24.3 % (46/189)	11.2 % (44/393)
TVR, CABG	4.2 % (8/189)	3.6 % (14/393)
TLR, Overall	24.3 % (46/189)	13.0 % (51/393)
TLR, PCI	22.8 % (43/189)	9.9 % (39/393)
TLR, CABG	4.2 % (8/189)	3.3 % (13/393)
Non-TLR TVR, Overall	6.9 % (13/189)	5.1 % (20/393)
Non-TLR TVR, PCI	5.8 % (11/189)	4.3 % (17/393)
Non-TLR TVR, CABG	1.6 % (3/189)	1.0 % (4/393)
Cardiac Death or MI	13.8 % (26/189)	9.4 % (37/393)
TLF	28.6 % (54/189)	18.1 % (71/393)
TVF	30.2 % (57/189)	18.6 % (73/393)
ARC ISR Stent Thrombosis Related to Target Lesion	3.7 % (7/189)	0.3 % (1/393)
Definite	3.2 % (6/189)	0.0 % (0/393)
Probable	0.0 % (0/189)	0.0 % (0/393)

Note: Events are based on CEC adjudication and MI is a composite event per SCAI definition for peri-procedural MI and the 4th Universal definition for spontaneous MI.
Note: Events that occurred within 365 days post procedure are included in the analysis.

Overall MI rate through 12 months, including periprocedural and spontaneous, for the primary trial definition and alternative definitions are shown in **Table 11**.

Table 11: MI Through 12 Months – MI Rates Using Alternative Definitions, ITT (N=600)

Events	POBA (N=194)	AGENT DCB (N=406)
Total Evaluable Subjects	189	393
MI (Primary trial definition)	12.2 % (23/189)	7.4 % (29/393)
Periprocedural (SCAI definition, ≤ 48 hours after index procedure)	2.6 % (5/189)	1.5 % (6/393)
Spontaneous (4th Universal definition, > 48 hours after index procedure)	9.5 % (18/189)	6.1 % (24/393)
MI (4th Universal definition)	11.1 % (21/189)	7.6 % (30/393)
Periprocedural (≤ 48 hours after index procedure)	1.6 % (3/189)	1.8 % (7/393)
Spontaneous (> 48 hours after index procedure)	9.5 % (18/189)	6.1 % (24/393)
MI (ARC-2 definition)	10.6 % (20/189)	7.6 % (30/393)
Periprocedural (≤ 48 hours after index procedure)	1.1 % (2/189)	1.8 % (7/393)
Spontaneous (> 48 hours after index procedure)	9.5 % (18/189)	6.1 % (24/393)
Note: Events that occurred within 365 days post procedure are included in the analysis.		

All site-reported serious adverse events are presented in **Table 12**.

Table 12: Site-Reported Serious Adverse Events Through 1-Year, ITT (N=600)

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
Total	**Total**	**Total**	**306**	**58.2% (113/194)**	**623**	**55.7% (226/406)**
Cardiac disorders	**Total**	**Total**	**132**	**38.7% (75/194)**	**238**	**35.0% (142/406)**
	Coronary artery disorders	**Total**	**98**	**33.0% (64/194)**	**153**	**28.8% (117/406)**
		Angina unstable	36	12.9% (25/194)	43	8.6% (35/406)
		Angina pectoris	28	11.9% (23/194)	43	9.9% (40/406)
		Acute myocardial infarction	16	7.2% (14/194)	25	5.2% (21/406)
		Coronary artery disease	12	5.7% (11/194)	21	5.2% (21/406)
		Myocardial infarction	2	1.0% (2/194)	7	1.7% (7/406)
		Acute coronary syndrome	2	1.0% (2/194)	5	1.2% (5/406)
		Other	2	1.0% (2/194)	9	2.2% (9/406)
	Heart failures	**Total**	**20**	**7.7% (15/194)**	**35**	**5.9% (24/406)**
		Cardiac failure	2	1.0% (2/194)	17	2.5% (10/406)
		Cardiac failure congestive	10	4.1% (8/194)	8	1.7% (7/406)
		Cardiac failure acute	4	2.1% (4/194)	3	0.7% (3/406)
		Left ventricular failure	2	1.0% (2/194)	3	0.7% (3/406)
		Other	2	1.0% (2/194)	4	1.0% (4/406)
	Cardiac arrhythmias	**Total**	**9**	**4.6% (9/194)**	**39**	**6.4% (26/406)**
		Atrial fibrillation	5	2.6% (5/194)	16	3.4% (14/406)
		Other	4	2.1% (4/194)	23	3.9% (16/406)
		Total	**2**	**1.0% (2/194)**	**4**	**1.0% (4/406)**

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
	Cardiac valve disorders	Other	2	1.0% (2/194)	4	1.0% (4/406)
	Myocardial disorders	**Total**	**2**	**1.0% (2/194)**	**4**	**1.0% (4/406)**
		Cardiomyopathy	2	1.0% (2/194)	0	0.0% (0/406)
		Other	0	0.0% (0/194)	4	1.0% (4/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**3**	**0.5% (2/406)**
		Other	1	0.5% (1/194)	3	0.5% (2/406)
Infections and infestations	**Total**	**Total**	**20**	**7.7% (15/194)**	**50**	**10.1% (41/406)**
	Infections - pathogen unspecified	**Total**	**13**	**4.6% (9/194)**	**36**	**7.4% (30/406)**
		Pneumonia	5	2.6% (5/194)	10	2.2% (9/406)
		Urinary tract infection	2	1.0% (2/194)	3	0.7% (3/406)
		Other	6	3.1% (6/194)	23	4.9% (20/406)
	Viral infectious disorders	**Total**	**5**	**2.6% (5/194)**	**6**	**1.5% (6/406)**
		COVID-19	2	1.0% (2/194)	3	0.7% (3/406)
		COVID-19 pneumonia	2	1.0% (2/194)	2	0.5% (2/406)
		Other	1	0.5% (1/194)	1	0.2% (1/406)
	Bacterial infectious disorders	**Total**	**2**	**1.0% (2/194)**	**8**	**2.0% (8/406)**
		Cellulitis	2	1.0% (2/194)	3	0.7% (3/406)
		Other	0	0.0% (0/194)	5	1.2% (5/406)
General disorders and administration site conditions	**Total**	**Total**	**19**	**8.2% (16/194)**	**38**	**8.1% (33/406)**
	General system disorders NEC	**Total**	**11**	**4.1% (8/194)**	**24**	**5.7% (23/406)**
		Non-cardiac chest pain	5	2.6% (5/194)	11	2.7% (11/406)
		Chest pain	4	1.5% (3/194)	5	1.2% (5/406)
		Other	2	1.0% (2/194)	8	2.0% (8/406)
	Complications associated with device	**Total**	**5**	**2.6% (5/194)**	**6**	**1.5% (6/406)**
		Vascular stent stenosis	3	1.5% (3/194)	5	1.2% (5/406)
		Vascular stent thrombosis	2	1.0% (2/194)	0	0.0% (0/406)
		Other	0	0.0% (0/194)	1	0.2% (1/406)
	Administration site reactions	**Total**	**2**	**1.0% (2/194)**	**5**	**1.2% (5/406)**
		Other	2	1.0% (2/194)	5	1.2% (5/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**3**	**0.7% (3/406)**
		Other	1	0.5% (1/194)	3	0.7% (3/406)
Vascular disorders	**Total**	**Total**	**19**	**8.2% (16/194)**	**28**	**6.2% (25/406)**
	Decreased and nonspecific blood pressure disorders and shock	**Total**	**4**	**2.1% (4/194)**	**12**	**3.0% (12/406)**
		Hypotension	3	1.5% (3/194)	8	2.0% (8/406)
		Other	1	0.5% (1/194)	4	1.0% (4/406)
	Arteriosclerosis, stenosis, vascular insufficiency and necrosis	**Total**	**5**	**2.6% (5/194)**	**8**	**1.5% (6/406)**
		Aortic stenosis	2	1.0% (2/194)	2	0.5% (2/406)
		Peripheral arterial occlusive disease	2	1.0% (2/194)	1	0.2% (1/406)
		Other	1	0.5% (1/194)	5	1.0% (4/406)
		Total	**5**	**2.6% (5/194)**	**4**	**1.0% (4/406)**

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
	Vascular hypertensive disorders	Hypertension	4	2.1% (4/194)	3	0.7% (3/406)
		Other	1	0.5% (1/194)	1	0.2% (1/406)
	Vascular haemorrhagic disorders	**Total**	**3**	**1.5% (3/194)**	**0**	**0.0% (0/406)**
		Haematoma	3	1.5% (3/194)	0	0.0% (0/406)
	Other	**Total**	**2**	**1.0% (2/194)**	**4**	**1.0% (4/406)**
		Other	2	1.0% (2/194)	4	1.0% (4/406)
Respiratory, thoracic and mediastinal disorders	**Total**	**Total**	**23**	**8.2% (16/194)**	**45**	**5.9% (24/406)**
	Respiratory disorders NEC	**Total**	**9**	**4.1% (8/194)**	**21**	**3.4% (14/406)**
		Acute respiratory failure	3	1.5% (3/194)	8	1.0% (4/406)
		Dyspnoea	3	1.5% (3/194)	6	1.5% (6/406)
		Other	3	1.5% (3/194)	7	1.5% (6/406)
	Bronchial disorders (excl neoplasms)	**Total**	**6**	**3.1% (6/194)**	**12**	**1.5% (6/406)**
		Chronic obstructive pulmonary disease	4	2.1% (4/194)	10	1.2% (5/406)
		Other	2	1.0% (2/194)	2	0.5% (2/406)
	Lower respiratory tract disorders (excl obstruction and infection)	**Total**	**2**	**1.0% (2/194)**	**6**	**1.5% (6/406)**
		Pulmonary oedema	2	1.0% (2/194)	2	0.5% (2/406)
		Other	0	0.0% (0/194)	4	1.0% (4/406)
	Pulmonary vascular disorders	**Total**	**3**	**1.5% (3/194)**	**1**	**0.2% (1/406)**
		Pulmonary embolism	2	1.0% (2/194)	0	0.0% (0/406)
		Other	1	0.5% (1/194)	1	0.2% (1/406)
	Pleural disorders	**Total**	**2**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
		Pleural effusion	2	1.0% (2/194)	2	0.5% (2/406)
		Other	0	0.0% (0/194)	1	0.2% (1/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**2**	**0.5% (2/406)**
		Other	1	0.5% (1/194)	2	0.5% (2/406)
Nervous system disorders	**Total**	**Total**	**21**	**7.7% (15/194)**	**29**	**6.4% (26/406)**
	Neurological disorders NEC	**Total**	**7**	**3.6% (7/194)**	**11**	**2.7% (11/406)**
		Syncope	2	1.0% (2/194)	3	0.7% (3/406)
		Presyncope	2	1.0% (2/194)	1	0.2% (1/406)
		Other	3	1.5% (3/194)	7	1.7% (7/406)
	Central nervous system vascular disorders	**Total**	**8**	**3.6% (7/194)**	**6**	**1.5% (6/406)**
		Cerebrovascular accident	4	2.1% (4/194)	2	0.5% (2/406)
		Other	4	1.5% (3/194)	4	1.0% (4/406)
	Other	**Total**	**6**	**2.6% (5/194)**	**12**	**2.7% (11/406)**
		Other	6	2.6% (5/194)	12	2.7% (11/406)
Injury, poisoning and	**Total**	**Total**	**15**	**6.7% (13/194)**	**30**	**5.9% (24/406)**
		Total	**7**	**3.6% (7/194)**	**11**	**2.2% (9/406)**
		Plaque shift	2	1.0% (2/194)	3	0.7% (3/406)

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
procedural complications	**Procedural related injuries and complications NEC**	Vascular pseudoaneurysm	2	1.0% (2/194)	0	0.0% (0/406)
		Other	3	1.5% (3/194)	8	1.5% (6/406)
	Injuries NEC	**Total**	**4**	**2.1% (4/194)**	**13**	**3.0% (12/406)**
		Fall	2	1.0% (2/194)	3	0.7% (3/406)
		Other	2	1.0% (2/194)	10	2.5% (10/406)
	Bone and joint injuries	**Total**	**4**	**2.1% (4/194)**	**5**	**0.7% (3/406)**
		Humerus fracture	2	1.0% (2/194)	0	0.0% (0/406)
		Other	2	1.0% (2/194)	5	0.7% (3/406)
	Other	**Total**	**0**	**0.0% (0/194)**	**1**	**0.2% (1/406)**
		Other	0	0.0% (0/194)	1	0.2% (1/406)
Gastrointestinal disorders	**Total**	**Total**	**12**	**5.2% (10/194)**	**38**	**5.4% (22/406)**
	Gastrointestinal haemorrhages NEC	**Total**	**0**	**0.0% (0/194)**	**9**	**1.7% (7/406)**
		Other	0	0.0% (0/194)	9	1.7% (7/406)
	Gastrointestinal signs and symptoms	**Total**	**2**	**0.5% (1/194)**	**8**	**1.2% (5/406)**
		Other	2	0.5% (1/194)	8	1.2% (5/406)
	Gastrointestinal stenosis and obstruction	**Total**	**2**	**1.0% (2/194)**	**5**	**0.7% (3/406)**
		Other	2	1.0% (2/194)	5	0.7% (3/406)
	Dental and gingival conditions	**Total**	**2**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
		Dental caries	2	1.0% (2/194)	2	0.5% (2/406)
		Other	0	0.0% (0/194)	1	0.2% (1/406)
	Abdominal hernias and other abdominal wall conditions	**Total**	**2**	**1.0% (2/194)**	**2**	**0.5% (2/406)**
		Other	2	1.0% (2/194)	2	0.5% (2/406)
	Diverticular disorders	**Total**	**2**	**1.0% (2/194)**	**0**	**0.0% (0/406)**
		Other	2	1.0% (2/194)	0	0.0% (0/406)
	Other	**Total**	**2**	**1.0% (2/194)**	**11**	**2.2% (9/406)**
		Other	2	1.0% (2/194)	11	2.2% (9/406)
Renal and urinary disorders	**Total**	**Total**	**6**	**3.1% (6/194)**	**27**	**5.4% (22/406)**
	Renal disorders (excl nephropathies)	**Total**	**3**	**1.5% (3/194)**	**15**	**3.0% (12/406)**
		Acute kidney injury	3	1.5% (3/194)	12	2.5% (10/406)
		Other	0	0.0% (0/194)	3	0.7% (3/406)
	Urinary tract signs and symptoms	**Total**	**2**	**1.0% (2/194)**	**6**	**1.5% (6/406)**
		Urinary retention	0	0.0% (0/194)	5	1.2% (5/406)
		Other	2	1.0% (2/194)	1	0.2% (1/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**6**	**1.5% (6/406)**
		Other	1	0.5% (1/194)	6	1.5% (6/406)
Metabolism and nutrition disorders	**Total**	**Total**	**11**	**4.1% (8/194)**	**23**	**3.7% (15/406)**
		Total	**5**	**2.6% (5/194)**	**6**	**1.5% (6/406)**
		Hyperglycaemia	5	2.6% (5/194)	3	0.7% (3/406)

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
	Glucose metabolism disorders (incl diabetes mellitus)	Other	0	0.0% (0/194)	3	0.7% (3/406)
	Electrolyte and fluid balance conditions	**Total**	**3**	**1.0% (2/194)**	**6**	**1.2% (5/406)**
		Hypokalaemia	2	1.0% (2/194)	1	0.2% (1/406)
		Other	1	0.5% (1/194)	5	1.2% (5/406)
	Acid-base disorders	**Total**	**3**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
		Other	3	1.0% (2/194)	3	0.7% (3/406)
	Other	**Total**	**0**	**0.0% (0/194)**	**8**	**1.2% (5/406)**
		Other	0	0.0% (0/194)	8	1.2% (5/406)
Blood and lymphatic system disorders	**Total**	**Total**	**7**	**3.6% (7/194)**	**16**	**3.7% (15/406)**
	Anaemias nonhaemolytic and marrow depression	**Total**	**5**	**2.6% (5/194)**	**11**	**2.7% (11/406)**
		Anaemia	5	2.6% (5/194)	7	1.7% (7/406)
		Other	0	0.0% (0/194)	4	1.0% (4/406)
	Platelet disorders	**Total**	**2**	**1.0% (2/194)**	**1**	**0.2% (1/406)**
		Heparin-induced thrombocytopenia	2	1.0% (2/194)	0	0.0% (0/406)
		Other	0	0.0% (0/194)	1	0.2% (1/406)
	Other	**Total**	**0**	**0.0% (0/194)**	**4**	**1.0% (4/406)**
		Other	0	0.0% (0/194)	4	1.0% (4/406)
Musculoskeletal and connective tissue disorders	**Total**	**Total**	**5**	**2.6% (5/194)**	**13**	**3.0% (12/406)**
	Joint disorders	**Total**	**2**	**1.0% (2/194)**	**7**	**1.5% (6/406)**
		Other	2	1.0% (2/194)	7	1.5% (6/406)
	Musculoskeletal and connective tissue deformities (incl intervertebral disc disorders)	**Total**	**2**	**1.0% (2/194)**	**2**	**0.5% (2/406)**
		Cervical spinal stenosis	2	1.0% (2/194)	0	0.0% (0/406)
		Other	0	0.0% (0/194)	2	0.5% (2/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**4**	**1.0% (4/406)**
		Other	1	0.5% (1/194)	4	1.0% (4/406)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**Total**	**Total**	**4**	**2.1% (4/194)**	**11**	**2.5% (10/406)**
	Gastrointestinal neoplasms malignant and unspecified	**Total**	**2**	**1.0% (2/194)**	**1**	**0.2% (1/406)**
		Other	2	1.0% (2/194)	1	0.2% (1/406)
	Other	**Total**	**2**	**1.0% (2/194)**	**10**	**2.5% (10/406)**
		Other	2	1.0% (2/194)	10	2.5% (10/406)
Investigations	**Total**	**Total**	**3**	**1.5% (3/194)**	**13**	**2.0% (8/406)**
	Microbiology and serology investigations	**Total**	**2**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
		SARS-CoV-2 test positive	2	1.0% (2/194)	3	0.7% (3/406)
	Other	**Total**	**1**	**0.5% (1/194)**	**10**	**1.2% (5/406)**
		Other	1	0.5% (1/194)	10	1.2% (5/406)
Eye disorders	**Total**	**Total**	**1**	**0.5% (1/194)**	**7**	**1.5% (6/406)**
	Other	**Total**	**1**	**0.5% (1/194)**	**7**	**1.5% (6/406)**
		Other	1	0.5% (1/194)	7	1.5% (6/406)

Serious Adverse Event			POBA (N=194 Subjects)		DCB (N=406 Subjects)	
MedDRA System Organ Class	**MedDRA High-Level Group Term**	**MedDRA Preferred Term**	**Events (n)**	**Percent of Subjects with Event (n/N)**	**Events (n)**	**Percent of Subjects with Event (n/N)**
Skin and subcutaneous tissue disorders	**Total**	**Total**	**2**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
	Other	**Total**	**2**	**1.0% (2/194)**	**3**	**0.7% (3/406)**
		Other	2	1.0% (2/194)	3	0.7% (3/406)
Immune system disorders	**Total**	**Total**	**2**	**1.0% (2/194)**	**0**	**0.0% (0/406)**
	Allergic conditions	**Total**	**2**	**1.0% (2/194)**	**0**	**0.0% (0/406)**
		Hypersensitivity	2	1.0% (2/194)	0	0.0% (0/406)
Other	**Total**	**Total**	**4**	**2.1% (4/194)**	**14**	**3.2% (13/406)**
	Other	**Total**	**4**	**2.1% (4/194)**	**14**	**3.2% (13/406)**
		Other	4	2.1% (4/194)	14	3.2% (13/406)

"Events" numbers are total episodes of each type of event among all patients.
"Percent of Subjects with Event" numbers are percent of patients who experienced one or more episodes of the event.
"Events" numbers for "TOTAL" are the sum of the individual event category totals.
"Percent of Subjects with Event" numbers for "TOTAL" is the percent of patients who experienced an adverse event.
Events with rate >1% in either arm are listed by preferred term; Otherwise, events are grouped in 'Other' Preferred term within each high-level group term.
The same logic as preferred term is applied to high-level group term and SOC term, the events with rate >1% in either arm are listed; Otherwise, the terms are grouped into 'Other' high-level group term and SOC term respectively.

Results in Various Subgroups

The AGENT IDE included pre-specified subgroups for gender (male and female), age (< 75 and ≥ 75 years), diabetic status, small vessel vs larger vessel (RVD < 2.75 mm and ≥ 2.75 mm), one stent layer restenosis and multiple stent layer restenosis (recurrent restenosis), target lesion only and target lesion plus 1 non-target lesion treated, BMS and DES restenosis, and CTO and non-CTO. The AGENT IDE was not designed or powered to study safety or effectiveness of the AGENT DCB versus POBA in the pre-specified subgroups, so these analyses are considered hypothesis-generating. The primary endpoint results for various subgroups are included in **Table 13** below.

The subgroup analyses mostly showed that the primary endpoint outcomes were similar within the various subgroups, including gender and vessel diameter. While no interaction was seen, the treatment effect with the AGENT DCB was numerically greater in older patients, non-diabetics, and in multiple stent layers. A significant interaction was noted in subjects who had a target lesion only vs a target lesion plus 1 non-target lesion, where the AGENT DCB had a significantly lower rate of TLF for target lesion treatment only (30.7 % POBA vs 17.4 % AGENT DCB) as compared to both target and non-target lesion treatment, where the AGENT DCB had a numerically higher TLF rate (15.4 % POBA vs 22.4 % AGENT DCB). It is important to note that the sample size was small (only n=77 subjects total had both a target and non-target lesion treatment), and this analysis was not powered.

Table 13: Primary Endpoint Results for Various Subgroups, Intent-to-Treat (N=600)

TLF at 12 Months	POBA (N=194)	AGENT DCB (N=406)	Relative Risk [95 % CI]	Difference [95 % CI]	P-value	Interaction P-value
Female (N=157)	(N=53)	(N=104)				0.9067
	23.5 % (12/51)	13.9 % (14/101)	0.59 [0.29, 1.18]	-9.7 % [-23.1 %, 3.8 %]	0.1350	
Male (N=443)	(N=141)	(N=302)				
	30.4 % (42/138)	19.5 % (57/292)	0.64 [0.46, 0.90]	-10.9 % [-19.8 %, -2.0 %]	0.0121	
Age < 75 years (N=436)	(N=139)	(N=297)				0.3223
	27.6 % (37/134)	19.2 % (55/286)	0.70 [0.48, 1.00]	-8.4 % [-17.2 %, 0.5 %]	0.0529	

TLF at 12 Months	POBA (N=194)	AGENT DCB (N=406)	Relative Risk [95 % CI]	Difference [95 % CI]	P-value	Interaction P-value
Age ≥ 75 years (N=164)	(N=55)	(N=109)				
	30.9 % (17/55)	15.0 % (16/107)	0.48 [0.27, 0.88]	-16.0 % [-29.9 %, -2.0 %]	0.0169	
Diabetics§ (N=269)	(N=90)	(N=179)				
	29.5 % (26/88)	22.1 % (38/172)	0.75 [0.49, 1.15]	-7.5% [-18.8 %, 3.9 %]	0.1868	0.3619
Non-Diabetics* (N=329)	(N=104)	(N=225)				
	27.7 % (28/101)	15.1 % (33/219)	0.54 [0.35, 0.85]	-12.7 % [-22.6 %, -2.7 %]	0.0074	
Small Vessel (RVD < 2.75 mm) (N=332)	(N=101)	(N=231)				
	28.1 % (27/96)	17.3 % (39/225)	0.62 [0.40, 0.95]	-10.8 % [-21.1 %, -0.5 %]	0.0285	0.9095
Large Vessel (RVD ≥ 2.75 mm) (N=265)	(N=91)	(N=174)				
	29.7 % (27/91)	19.2 % (32/167)	0.65 [0.41, 1.01]	-10.5 % [-21.6 %, 0.6 %]	0.0548	
Single Stent Layer† (N=341)	(N=112)	(N=229)				
	20.2 % (22/109)	13.6 % (30/220)	0.68 [0.41, 1.11]	-6.5 % [-15.3 %, 2.2 %]	0.1255	0.5010
Multiple Stent Layer† (N=258)	(N=82)	(N=176)				
	40.0 % (32/80)	23.8 % (41/172)	0.60 [0.41, 0.87]	-16.2 % [-28.6 %, -3.7 %]	0.0085	
Target Lesion Treatment Only†† (N=523)	(N=168)	(N=355)				
	30.7 % (50/163)	17.4 % (60/344)	0.57 [0.41, 0.79]	-13.2 % [-21.4 %, -5.1 %]	0.0007	
Both Target and Non Target Lesion Treatment†† (N=77)	(N=26)	(N=51)				0.0763
	15.4 % (4/26)	22.4 % (11/49)	1.46 [0.52, 4.13]	7.1 % [-11.1 %, 25.2 %]	0.4667	
History of DES Treatment Only‡ (N=527)	(N=171)	(N=356)				
	29.9 % (50/167)	18.7 % (64/343)	0.62 [0.45, 0.86]	-11.3 % [-19.4 %, -3.2 %]	0.0041	
History of Both DES and BMS Treatment‡ (N=19)	(N=6)	(N=13)				
	60.0 % (3/5)	38.5 % (5/13)	0.64 [0.24, 1.73]	-21.5 % [N/A]	0.6078*	0.9735
History of BMS Treatment Only (N=38)	(N=9)	(N=29)				
	0.0 % (0/9)	6.9 % (2/29)	Undef [Undef, Undef]	6.9 % [N/A]	1.0000*	
Total Occlusion (N=14)	(N=5)	(N=9)				
	20.0 % (1/5)	22.2 % (2/9)	1.11 [0.13, 9.42]	2.2 % [N/A]	1.0000*	0.5815
Non-Total Occlusion (N=582)	(N=186)	(N=396)				
	29.3 % (53/181)	18.0 % (69/383)	0.62 [0.45, 0.84]	-11.3 % [-18.9 %, -3.6 %]	0.0024	
History of DES Treatment Only (N=527)	(N=171)	(N=356)				
	29.9 % (50/167)	18.7 % (64/343)	0.62 [0.45, 0.86]	-11.3% [-19.4 %, -3.2 %]	0.0041	0.6973
History of Any BMS Treatment (N=57)	(N=15)	(N=42)				
	21.4 % (3/14)	16.7 % (7/42)	0.78 [0.23, 2.61]	-4.8 % [NA]	0.6984*	

TLF at 12 Months	POBA (N=194)	AGENT DCB (N=406)	Relative Risk [95 % CI]	Difference [95 % CI]	P-value	Interaction P-value

P-values are two-sided from Fisher's exact test; P-values without * are from the Chi-square test. The p-values have not been adjusted for multiplicity.
'Interaction P-value' tests the treatment by subgroup interaction from logistic regression. An interaction p-value of 0.15 was considered a significant interaction.
§Diabetic subgroup includes diabetic subjects requiring medical treatment (oral or injection) for control of blood glucose levels. Non-diabetics subgroup includes diabetic subjects treated with diet only or subjects without diabetes.
RVD is based on angio core lab data.
†Refers to subjects with single stent layer restenosis treatment or subjects with multiple stent layer restenosis treatment.
††Refers to subjects with Target Lesion Treatment Only or subjects with Both Target and Non Target Lesion Treatment.

Human Pharmacokinetics

A human pharmacokinetic (PK) sub-study was not conducted for the AGENT DCB. Since pre-clinical PK data suggested that the drug was present at low levels in the blood and cleared rapidly, the possible systemic drug exposure of the AGENT DCB in humans based on the intended use is expected to be low with limited safety concerns. Therefore, it was determined that human PK data was not needed to mitigate any risks due to the systemic exposure of the drug from the AGENT DCB.

HOW SUPPLIED

Device Details

Contents supplied STERILE using an ethylene oxide (EO) process.

Do not use if package is opened or damaged. Do not use if labeling is incomplete or illegible.

Handling and Storage

Store at 25 °C (77 °F); excursions permitted to 15 °C - 30 °C (59 °F- 86 °F).

OPERATIONAL INSTRUCTIONS

One or more of each of the following materials are required for drug-coated balloon PCI with the AGENT Drug-Coated Balloon Catheter:

- Guidewire of appropriate size for advancement of guide catheter.
- Arterial sheath and dilator.
- Guide catheter in the appropriate size and configuration to canulate the coronary artery.
- Contrast media.
- Sterile saline.
- Inflation device with manometer.
- PTCA balloon catheter and/or interventional equipment (including intravascular imaging) required for pre-treatment and lesion preparation.
- 0.014 in guidewire.
- 10 ml, 12 ml, or 20 ml (cc) luer-lock syringe.
- Hemostatic (Tuohy-Borst) valve.
- Three-way stopcock.

Preparation

Inspection Prior to Use

Prior to drug-coated balloon PCI, carefully examine all equipment to be used during the procedure, including the AGENT Drug-Coated Balloon Catheter, to verify proper function. Verify the catheter and sterile packaging have not been damaged. Verify the catheter size is suitable for the intended procedure.

Do not use if sterile package is damaged.

Caution: Damage to the device's drug coating or premature release of the drug may occur if the drug-coated balloon is touched, wiped, bent, squeezed, or comes into contact with any liquids prior to insertion.

Note: Do not use the drug-coated balloon catheter if damage occurs or sterility is compromised.

Inflation Device Preparation

1. Prepare the inflation device according to the manufacturer's instructions.
2. Purge the system of air.

AGENT Drug-Coated Balloon Catheter Selection

The inflation diameter of the drug-coated balloon catheter should not exceed the diameter of the coronary artery proximal and distal to the treatment area. Similarly, the inflated length of the drug-coated balloon (shoulder to shoulder) should minimally overlap the length of the lesion within the coronary artery.

Caution: The AGENT DCB is indicated for lesions up to 26 mm using one balloon. The safety and effectiveness of treating lesions longer than 26 mm has not been established. When clinically warranted, if there is the need to treat a lesion longer than the maximum balloon length available, each individual segment should be treated with a single inflation using the AGENT Drug-Coated Balloon. Treat each segment with a new balloon; try to minimize overlapping the treated segments.

AGENT Drug-Coated Balloon Catheter Preparation

Caution: It is recommended to adequately prepare the vessel to facilitate passage of the drug-coated balloon catheter.

1. Remove the drug-coated balloon catheter from its protective coil. Use care when removing the catheter to avoid damage (e.g., shaft kink).
2. The drug-coated balloon catheter may be coiled once and secured using the CLIPIT clip provided in the catheter package. Only the proximal shaft should be inserted into the clip; the clip is not intended for the distal end of the balloon catheter. Remove the clip prior to inserting the balloon catheter into the patient.
   Note: Care should be taken not to kink the shaft of the balloon catheter upon application or removal of the CLIPIT clip.
3. Prepare the balloon catheter for purging. Fill a 10 ml, 12 ml, or 20 ml luer-lock syringe with inflation medium.
   Warning: Use only the recommended inflation medium (50:50 mixture of contrast medium and sterile saline solution). Never use air or any gaseous medium through the inflation port.
4. Connect a three-way stopcock to the catheter inflation port. Close the stopcock to the drug-coated balloon catheter and flush through the stopcock. Use care when connecting the catheter to avoid damage (e.g., shaft kink).
5. Connect the inflation device to the stopcock. Assure luer connections are properly aligned to avoid stripping the luer thread and causing subsequent leakage. Use care when connecting the drug-coated balloon catheter to avoid damage (e.g., shaft kink).
6. Hold the inflation device with the nozzle pointing downward and aspirate for 5 seconds. Release the plunger or open the stopcock to air.
7. Disconnect the inflation device and evacuate all air from the barrel.
8. To prevent the possibility of air embolism, reconnect the inflation device and aspirate for 5 seconds until bubbles no longer appear. If bubbles persist, check the luer connections. Discard and replace the AGENT Drug-Coated Balloon Catheter if the leak cannot be resolved.
9. To remove any air lodged in the distal luer fitting of the inflation device, purge approximately 1 ml (cc) of inflation medium while pointing the inflation device upwards.
10. Disconnect the inflation device used in preparation. Verify that a meniscus of the inflation medium is evident in both the inflation port and the inflation device connection to ensure a fluid-to-fluid connection. Adding a drop of inflation medium to the port may be necessary. Securely couple the inflation device to the inflation port of the catheter.
11. Open the stopcock to the catheter and lock the system balloon to a negative pressure.
12. Remove the balloon protector and mandrel by grasping the catheter just proximal to the proximal balloon catheter bond site. With the other hand, gently grasp the distal section of the balloon protector and remove distally. Remove the mandrel distally after removing the balloon protector.

Caution: Do not pull the balloon protector proximally onto the catheter shaft.

Caution: If unusual resistance is felt during removal of the balloon protector or mandrel, do not use the AGENT Drug-Coated Balloon Catheter and replace with another.

Procedure

Insertion Procedure

Note: For optimal DCB results, adequate lesion preparation is essential. This should include pre-dilatation with a non-coated coronary balloon. Intravascular imaging to guide lesion preparation and to assess the adequacy of the final result is strongly recommended.

Caution: Lesion preparation is necessary to prevent delamination of the balloon's drug coating while traversing patient anatomy. The TransPax coating is designed to facilitate drug transfer into the vessel wall upon contact. Do not use the AGENT Drug-Coated Balloon Catheter for lesion preparation.

1. Drug-Coated Balloon Catheter Advancement
    A. Access and cross the stenosis with a 0.014 in guidewire using standard practice and/or manufacturer's instructions.
    B. After appropriate lesion preparation, thoroughly aspirate and flush the guide catheter in preparation for the AGENT Drug-Coated Balloon Catheter.
    Note: It is recommended to always use a smaller diameter balloon dilation catheter to pre-dilate the stenosis to facilitate passage of the drug-coated balloon catheter.
    C. Backload the distal tip of the drug-coated balloon catheter onto the guidewire ensuring the guidewire exits the wire port of the catheter manifold.
    Caution: Do not touch, wipe, bend, squeeze the drug-coated balloon, or allow it to come into contact with any liquids prior to insertion. Damage to the balloon drug coating or premature release of the drug may occur.
    Note: To avoid kinking, advance the catheter slowly, in small increments, until the proximal end of the guidewire emerges from the catheter.
    D. Carefully advance the drug-coated balloon catheter through the guiding catheter.
    Caution: When loading or exchanging the AGENT Drug-Coated Balloon device, it is recommended to
    thoroughly wipe the guidewire with sterile saline to facilitate catheter movement.
    Caution: Do not touch, wipe, bend, squeeze the drug-coated balloon or allow it to come into contact with any liquids prior to insertion. Damage to the balloon drug coating or premature release of the drug may occur.
    E. Thoroughly aspirate and flush the guide catheter in preparation for introduction of the balloon catheter.
    Note: It is recommended to always use a smaller diameter balloon dilation catheter to pre-dilate the stenosis to facilitate passage of the drug-coated balloon catheter.
    Caution: If unusual resistance is felt, do not advance the device. Never tighten the hemostatic valve onto the drug-coated balloon.
    Caution: If using a Tuohy-Borst type adapter, take care not to over-tighten the hemostatic valve around the catheter shaft as lumen constriction or catheter damage may occur, which may affect inflation/deflation of the device.
    F. Connect the side port of the guide catheter hemostatic valve to the proximal pressure recording/infusion line or manifold assembly.
    G. Under direct fluoroscopic visualization, advance the catheter over the guidewire and position the drug-coated balloon relative to the lesion to be treated. Use the radiopaque marker bands as reference points. The outside edges of the marker bands indicate the balloon shoulders. Balloon inflation should not be undertaken until the balloon is properly positioned within the treatment area.

2. Drug-Coated Balloon Inflation
    A. Carefully inflate the AGENT Drug-Coated Balloon to the desired pressure (refer to **Table 14**). Fluoroscopic visualization during treatment should be used to confirm adequate expansion to appose the balloon's drug coating with the treatment area. Maintain the desired inflation pressure for at least 30 seconds.
    Warning: Do not exceed the catheter rated burst pressure. Use of an inflation device with a manifold is recommended to prevent over-pressurization.
    Warning: If difficulty is experienced during the device's use, do not continue. Deflate the drug-coated balloon and remove the device.

B. Apply negative pressure to fully deflate the drug-coated balloon after drug transfer. Use fluoroscopy to confirm full deflation.
C. While maintaining guidewire position across the lesion, withdraw the AGENT Drug-Coated Balloon Catheter into the guiding catheter.
Note: Therapeutic drug dosage is administered only during the first inflation. Do not re-inflate the AGENT Drug-Coated Balloon Catheter.

3. Catheter Removal
A. Using angiography, confirm vessel patency and ensure the drug-coated balloon is fully deflated.
B. While maintaining negative pressure, withdraw the deflated drug-coated balloon catheter from the guide catheter through the hemostatic valve.
Warning: Do not advance or retract the catheter unless the balloon is fully deflated under vacuum. If unusual resistance is felt during manipulation, determine the cause of the resistance before proceeding. If the source of resistance cannot be determined, it is recommended to remove the entire system as a unit.

Table 14: AGENT Drug-Coated Balloon Compliance Chart

Pressure atm - kPa	Balloon Size (mm)						
	2.00	**2.25**	**2.50**	**2.75**	**3.00**	**3.50**	**4.00**
3.0 – 304	1.86	2.06	2.28	2.53	2.76	3.19	3.66
4.0 – 405	1.93	2.14	2.37	2.61	2.85	3.30	3.80
5.0 – 507	1.99	2.20	2.44	2.68	2.93	3.39	3.88
6.0 – 608	2.03	2.26	2.50	2.75	3.00	3.46	3.96
7.0 – 709	2.07	2.31	2.55	2.81	3.06	3.52	4.04
8.0 – 811	2.10	2.34	2.59	2.85	3.11	3.57	4.09
9.0 – 912	2.13	2.38	2.62	2.88	3.15	3.61	4.14
10.0 – 1013	2.15	2.40	2.65	2.91	3.18	3.64	4.18
11.0 – 1115	2.18	2.42	2.67	2.94	3.21	3.68	4.22
12.0 – 1216	2.19	2.44	2.69	2.96	3.23	3.72	4.25
13.0 – 1317	2.21	2.46	2.72	2.99	3.26	N/A	N/A
14.0 – 1419	2.23	2.48	2.74	3.02	3.28	N/A	N/A

*Nominal Pressure = 6 atm
**Rated Burst Pressure. DO NOT EXCEED

Disposal
To minimize the risk of infection or microbial hazards after use, dispose device and packaging as follows:

After use, device and packaging may contain biohazardous substances. Any device and packaging that came into contact with biohazardous substances should be treated and disposed of as biohazard waste or be treated and disposed of in accordance with any applicable hospital, administrative, and/or local government regulations. Use of a biohazardous container with biological hazard symbol is recommended. Untreated biohazardous waste should not be disposed of in the municipal waste system.

Post-Procedure
Any serious incident that occurs in relation to this device should be reported to the manufacturer and relevant local regulatory authority.

INFORMATION TO BRIEF THE PATIENT

The physician should consider the following points while counseling patients on the use of the AGENT Drug-Coated Balloon in association with drug-coated balloon PCI:

- Discuss the risks and benefits including review of potential adverse events listed in this document, both for the AGENT DCB and for other interventional or pharmacologic treatments likely to be employed.
- Discuss patient allergies, in particular, the risk for patients who may be allergic to paclitaxel, citrate, or contrast.
- Discuss the planned DAPT duration and the risks and benefits of anti-platelet therapy including risk of thrombosis should the patient prematurely discontinue use.
- Discuss post-procedure instructions, including any follow-up appointments, lifestyle changes, medications, and home-care or rehabilitation guidance.
- Advise the patient that additional information may be available on the Boston Scientific website (www.bostonscientific.com/patientlabeling).

WARRANTY

For device warranty information, visit **www.bostonscientific.com/warranty**.

Trademarks

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TAXOL is a trademark of Bristol-Myers Squibb Company.
All other trademarks are the property of their respective owners.

SYMBOL DEFINITIONS

Commonly used medical device symbols that appear on the labeling are defined at www.bostonscientific.com/SymbolsGlossary.
Additional symbols are defined at the end of this document.

Symbology Page

Catalog Number (REF)
ref1_s_c1t_l2_ag

Contents
contents1_s_c1t_l2_ag

Back Cover

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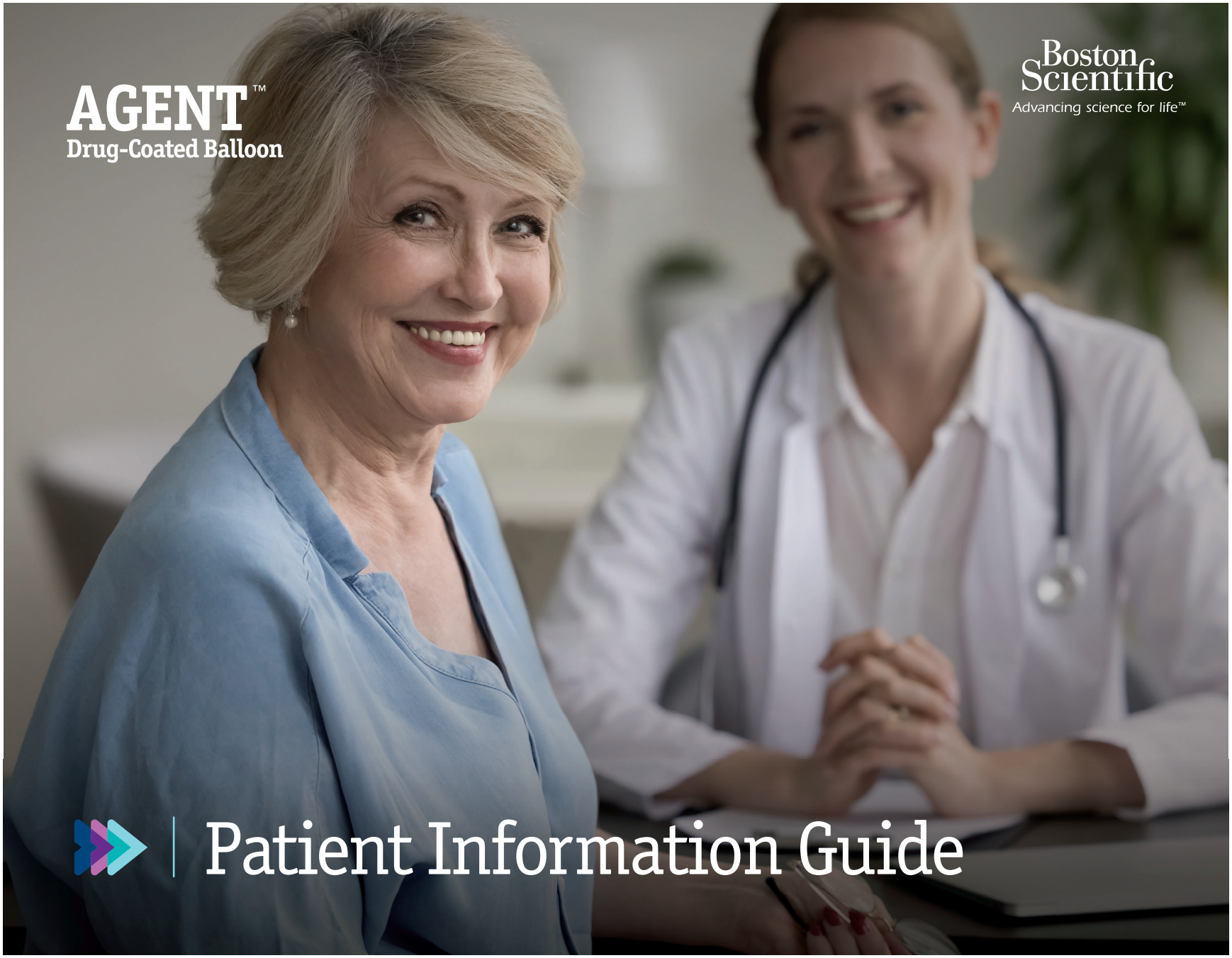

AGENT™
Drug-Coated Balloon

Boston Scientific
Advancing science for life™

Patient Information Guide

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Related professional use document: 51538498 01A

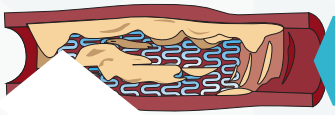
What is Coronary Artery Disease?

Coronary artery disease (CAD) affects the arteries that supply blood to the heart. It occurs when the coronary arteries become narrowed by a buildup of plaque, including cholesterol, fatty deposits, calcium, and other substances.

People who have high cholesterol, diabetes, smoking, high blood pressure, are overweight, or have a family history of heart disease are at higher risk of developing CAD. Menopause may also increase the risk of CAD in women. If you have been previously diagnosed with CAD, then you may have been treated with a stent. A stent helps keep the artery open.

What is In-Stent Restenosis (ISR)?

When a artery with a stent gets blocked or re-narrowed, it's called in-stent restenosis. In-stent restenosis (ISR) is re-narrowing caused by tissue from inflammation brought on during your previous Percutaneous Coronary Intervention (PCI).



The re-narrowing can be caused by a combination of factors including the blockage reforming or new tissue growth within the treated area.

What are the Treatment Options for ISR?

Management of in-stent restenosis (ISR) following implantation of a coronary stent is clinically challenging. The treatment options for ISR include:

Drug-Coated Balloon (DCB) PCI

Continued medical management

Open heart surgery for coronary artery bypass grafting (CABG)

Repeat balloon angioplasty or stent placement

Radiation including brachytherapy

What is the AGENT™ Drug-Coated Balloon?

The AGENT Drug-Coated Balloon is a balloon catheter with the drug paclitaxel applied to the balloon. The drug-coated balloon is inflated inside the blood vessel to allow drug transfer into the vessel wall to prevent re-narrowing.

What is paclitaxel?

Paclitaxel is a commonly used drug to treat blockages in blood vessels. Paclitaxel is the active drug component of the AGENT Drug-Coated Balloon. The AGENT Drug-Coated Balloon is coated with a small amount of paclitaxel. Paclitaxel is applied directly to the vessel wall when the balloon is inflated. This helps to reduce the amount of scar tissued formed.

Risks and Benefits

The AGENT™ Drug-Coated Balloon is intended to improve blood flow and treat blockages in previously placed stents. The AGENT Drug-Coated Balloon delivers drug to the vessel wall without implanting any new metal. Your doctor can help determine if you may be a good candidate for treatment with a drug-coated balloon.

Contraindications

The AGENT™ Drug-Coated Balloon should not be used if:

- You have a sensitivity to or have had an allergic reaction to paclitaxel
- The blockage to be treated is in an artery that is not in the heart
- The blockage to be treated is in the first part of the main artery supplying blood to left ventricle, the main pumping chamber of the heart
- Your blockage is a result of spasm of the artery
- You are unable to take the recommended medications prescribed for after the procedure
- You are pregnant, breastfeeding, planning to become pregnant or father a child
- If you are at risk, your doctor will choose another therapy for your CAD treatment.

Note: It is very common for your doctor to prescribe medications before, during, and after your procedure. These medications are intended to help decrease the risk of forming a blood clot in your artery. Please check with your doctor to find the right medication for you.

Risks and Benefits

Adverse Events

Potential adverse events (in alphabetical order) that may be associated with the use of AGENT Drug-Coated Balloon include, but are not limited to, the following:

- abnormal heart beats (that may become fatal)
- additional procedures that may include surgery
- allergic reaction to device or medicines used during the procedure
- bleeding
- blood build-up around the heart that prevents the heart from pumping
- closure of the treated blood vessel
- damage to the treated blood vessel that will require repair
- death
- fever/inflammation
- fragments of plaque, drug coating, blood clot or device that break off and travel down the blood stream
- heart attack
- heart failure, kidney failure, lung failure, liver failure
- infection, possibly in the blood (blood poisoning)
- low/high blood pressure
- pain, including chest pain from your heart or at incision site
- skin burns from the X-rays used during the procedure
- slow flow in the treated blood vessel
- stroke or mini-stroke

Potential adverse events not captured above, that have been associated with administration of paclitaxel at systemic doses, include, but are not limited to, the following:

- abnormal blood tests
- allergic reaction
- hair loss
- inflammation of blood vessels
- liver enzyme changes
- low blood cell count
- muscle or joint pain
- need for a blood transfusion
- nerve pain in arms or legs
- upset stomach

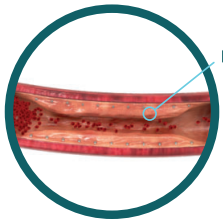
There may be other potential adverse events that are currently unforeseen. Apart from hypersensitivity reactions (allergic/immunologic reactions), the likelihood of paclitaxel related adverse events with AGENT use is low due to the low doses used on the balloon when compared to systemic chemotherapeutic doses. Any adverse event related to the AGENT Drug-Coated Balloon should be reported to Boston Scientific Corporation.

Benefits

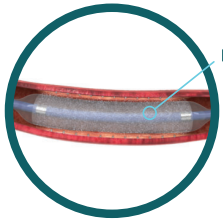
The AGENT™ Drug-Coated Balloon is designed to help re-open blocked arteries in the heart and to keep them open. The AGENT Drug-Coated Balloon also provides a benefit of not implanting another stent, which may allow for more options for future interventions, if needed.

What Happens During a Typical Drug-Coated Balloon Procedure?

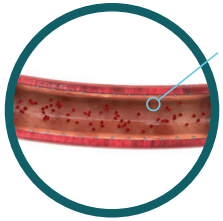
1. A small puncture is made in the patient's wrist and/or groin to gain access to the artery. A wire and catheter are inserted and moved to the narrowed section of the artery. The doctor will inject contrast dye into the artery to help see the artery.
2. The narrowed section of the artery will need to be enlarged to make room for the drug-coated balloon. To do this, the doctor will use other devices to push the plaque to the side or remove plaque buildup inside the artery.
3. When the doctor is satisfied with the opening of the narrowed blood vessel, the drug-coated balloon will be inserted.
4. After the drug-coated balloon is inserted, it is inflated to make contact with the artery wall, allowing the drug to be released. The devices are removed and the puncture site will be closed. The drug from the balloon is absorbed into the artery and is designed to help keep the artery open and prevent future narrowing of the artery.



Diseased Artery



Drug-Coated Balloon in the Artery



Result after Drug-Coated Balloon Procedure

After a Typical Drug-Coated Balloon Procedure

- You may feel sleepy from the sedative given to you. This will wear off over the next few hours.
- You will be taken to a unit where nurses and doctors can monitor you.
- Your vital signs (heart rate and blood pressure) and the catheter entry site will be checked frequently.
- You will be asked to drink plenty of liquids to flush the contrast dye out of your system. You will be asked to keep your leg or arm straight so the entry site can heal.
- You should alert your doctor or nurse if you experience any of these symptoms:
  - Reappearance of the symptoms you had before treatment
  - Pain, bleeding, or redness at the catheter entry site
- You should follow your doctor's instructions regarding your medications and activity level.
- You should keep all follow-up appointments requested by your doctor and bring your medications with you.

Living with Coronary Artery Disease

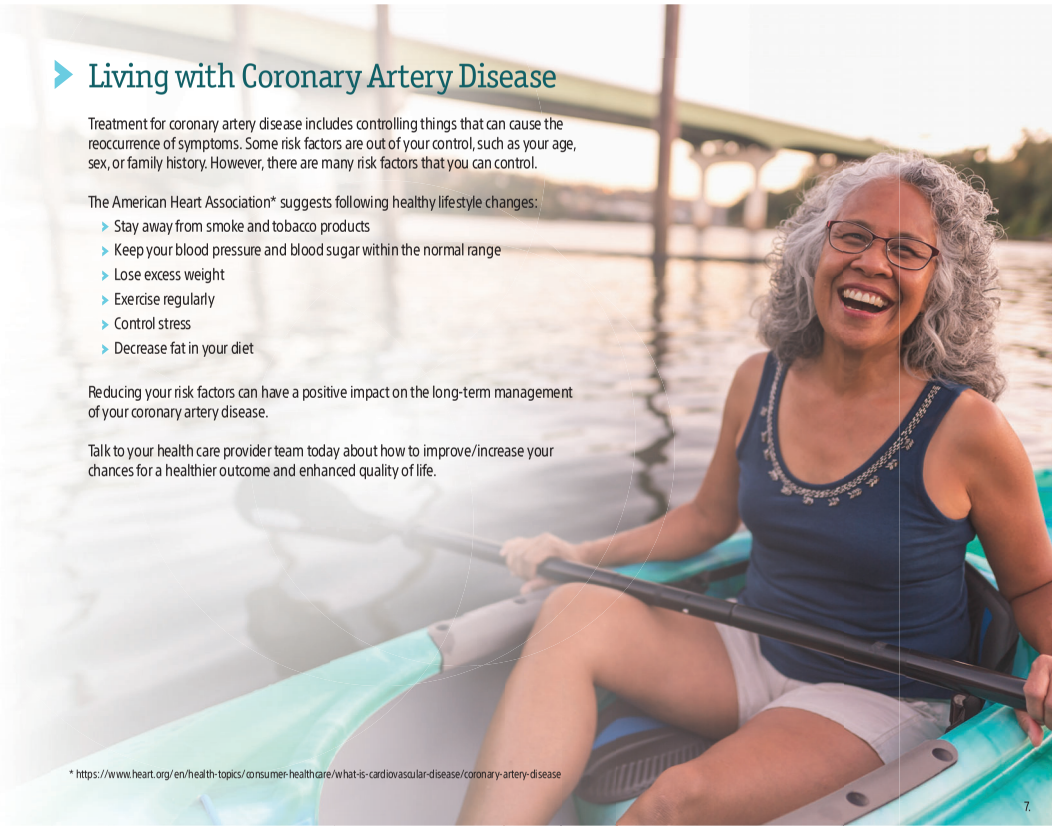
Treatment for coronary artery disease includes controlling things that can cause the reoccurrence of symptoms. Some risk factors are out of your control, such as your age, sex, or family history. However, there are many risk factors that you can control.

The American Heart Association* suggests following healthy lifestyle changes:

- Stay away from smoke and tobacco products
- Keep your blood pressure and blood sugar within the normal range
- Lose excess weight
- Exercise regularly
- Control stress
- Decrease fat in your diet

Reducing your risk factors can have a positive impact on the long-term management of your coronary artery disease.

Talk to your health care provider team today about how to improve/increase your chances for a healthier outcome and enhanced quality of life.



* https://www.heart.org/en/health-topics/consumer-healthcare/what-is-cardiovascular-disease/coronary-artery-disease

Clinical Data Summary

The AGENT™ Drug-Coated Balloon was evaluated in a clinical trial called the AGENT IDE study. The study enrolled 600 patients to determine if AGENT showed acceptable performance for long-term (12-month) safety and effectiveness.

The AGENT IDE study demonstrated that the AGENT Drug-Coated Balloon provided greater clinical benefit, including reducing the need for future procedures, compared to non-drug coated balloons.

The results also confirmed the AGENT Drug-Coated Balloon is safe and effective for treating in-stent restenosis in coronary arteries.

Glossary

Balloon Angioplasty
A procedure that can open up a blocked blood vessel using a small, flexible plastic tube, or catheter, with a balloon at the end of it. When the tube is in place, the balloon inflates to open the blood vessel, or artery, so that normal blood flow is restored

Balloon Catheter
A thin, flexible tube with a balloon attached to the tip that can be inflated inside the blood vessel

Coronary Artery
A blood vessel that carries oxygen-rich blood to the heart muscle

Coronary Artery Bypass Graft (CABG)
A surgical procedure used to create an alternate route for blood to flow to the heart around narrowed or blocked arteries

Contrast Dye
Injectable dye used to visualize blood vessels during X-ray procedures

Drug-Coated Balloon
A balloon that delivers a therapeutic drug dose directly to the vessel wall

Minimally Invasive Procedure
A procedure that uses small instruments or devices to reduce the size of the insertion site and cause a smaller amount of trauma

Paclitaxel
A drug that prevents vessel re-narrowing by limiting scar tissue

Percutaneous Coronary Intervention (PCI)
A broad set of procedures that are used to open up blocked coronary arteries such as balloon angioplasty, stent placement, or treatment with a drug-coated balloon

For more information about indications, contraindications, warnings and instructions for the AGENT™ Drug-Coated Balloon, or Patient Guide visit www.bostonscientific.com.

You may also call Boston Scientific customer service at 1.888.272.1001 for more information.

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