Supplemental Online Content

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This supplemental material has been provided by the authors to give readers additional information about their work.

AGENT IDE Investigators and Committees

eTable 1. AGENT IDE Investigators, Study Support, and Enrollment by Site Name

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
St. Francis Hospital	Roslyn, NY, USA	Shlofmitz	Richard	*Allen Jeremias, Evan Shlofmitz, George Petrossian, William Chung, Ziad Ali,* Ayyaz Sultan, Elizabeth Haag, Joan Jennings, Linda Bongiovanni, Lyn Santiago, Marion Cyriac, Meghan Murray, Patricia Krug, Sierra Beck, Tatiana Potylitsina	79
Columbia University Medical Center	New York, NY, USA	Moses	Jeffrey	*David Brogno, Megha Prasad, Michael Collins, Sahil Parikh, Tamin Nazif, Torsten Vahl, Vivian Ng, Ajay Kirtane, Gloria Weisz, Matthew Finn, Sanjum Sethi,* Alex Kantor, Andy Morales, Candido Batres, Jeimy Rosado, Kartik Kodali, Kate Dalton, Mildrid Duran, Sarah Myoung, Torsten Vahl	49
Pinnacle Health Cardiovascular Institute	Wormleysburg, PA, USA	Bachinsky	William	*Anay Pradhan, David Chang Cleon Hubbard, Torrey Schmidt,* Anisa Powis, Eric Diehl, Gretchen Meise, Joanna Miller, Laura Wells, Megan Alexander	41
Cedars - Sinai Medical Center	Los Angeles, CA, USA	Dohad	Suhail	Keren Sanchez-Cervantes, Kirin Bhatia	34
Lindner Center for Research and Education at Christ Hosp	Cincinnati, OH, USA	Rudick	Steven	*Puvi Seshiah, Dean Kereiakes, James Corl, James Kong, Jarrod Frizzell, Santiago Garcia, Satya Shreenivas, Timothy Henry, Timothy Smith* Allison Parvizi, Anne Voorhorst, Caroline Reed, Darlene Rock, David White, Deborah Garza, Debra Paige, Denise Krabbe, Elisabeth Schwartz, Emma Ries, Jessica Ackerman, Julianne O'Brien, Katherine Gloria, Linda Pennington, Mary Kreimer, Michael Weber, Samantha Tribble, Susan Reilly, Terri Sikora, Trent Rissover, Wendy Parker	31

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
Baylor Heart & Vascular Hospital	Dallas, TX, USA	Stoler	Robert	*James Choi, Ravi Vallabhan, Jeffrey Schussler, Zachary Rosol,* Angela Mendez, Angela Roy, Emily Liable, Geoffery Gong, Janet Dunkerley, Jennifer Cruthis, Kim Waters, Leslie Wilcott, Madison Byrd, Rebecca Baker, Susan Aston	30
Centennial Medical Center	Nashville, TN, USA	Jefferson	Brian	*Andrew Goodman, Ann Gage, Jeffrey Webber, Jonathan Riddick, Samuel Horr, Taral Patel,* Abdullah Shamsuddin, Abigayle Hanna, Drew Quillen, Molly Harper, Paul Dalecke	30
Emory University Hospital	Atlanta, GA, USA	Nicholson	William	*Chandon Devireddy, Gautam Kumar, Isida Byku, Khursow Niazi, Pratik Sanderesara, Wissam Jaber,* Amanda Fiebach, Claudia Merlin, Farhad Jameel, Jessica Navas-Simbana, Kyle Nadler, Mary Mungai, Riley Meehan, Wei Xu	28
St. Anthony Hospital	Denver, CO, USA	Altman	John	*Ahmad Alqaqa'a, Ashwin Murthy, David Halpin, Lawrence Laza, Nima Aghili* Alec Timp, Alexandra Kaleugher, David Bailey, Morgan Kothlow	20
Beth Israel Deaconess Medical Center	Boston, MA, USA	Yeh	Robert	*Eric Osborn, Eric Secemsky, Hector Tamez Aguilar, Mandeep Dhadly, Marie-France Poulin,* Hannah Hunsaker, Jenifer Kaufman, Lauren Lanuto, Patricia Tyler	16
South Denver Cardiology Associates, PC	Littleton, CO, USA	Bateman	Cinthia Tjan	*Erin Unger, Ira Dauber,* Andrea Kupser, Colleen Roccanova, Kathrin Siegel, Mary Soltau, Rebecca Wimmer	15
Cleveland Clinic Foundation	Cleveland, OH, USA	Krishnaswamy	Amar	*Grant Reed, Abraham Lincoff, Chris Bajzer, Claire Raphael, Jaikirshan Khatri, Khaled Ziada, Samir Kapadia, Stephen Ellis, Rishi Puri,* Aaron Jones, Adrienne Nadvornik, Aliyah Spates, Christina Stickan, Christine Comet, Emily Tylicki, Lydia Sweeney, Madalyn Espen, Marilyn Boros, Molly Savanick, Monica Branche, Nicole Boisvert,	15

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
				Rhonda Robinson-Gunther, Rita Brienza	
St. Luke's Hospital of Kansas City	Kansas City, MO, USA	Grantham	J. Aaron	*Dany Jacob, Adam Salisbury, Adnan Chhatriwalla, Anthony Hart, Chetan Huded, David Safley, Steven Laster,* Amanda Nesbitt, Dana King, Jamie Hall, Lisa Lacy, Megan Warden	14
Heart Hospital of Austin	Austin, TX, USA	Zidar	Francis	*Arthur Smith, Mark Picone, Matthew Selmon, Thomas McMinn, John Moscona, Juhana Karha,* Amanda Carpenter, Amanda Daniels, Jackie Narro, Katherine Nicholas, Kelly Stewart	13
Overland Park Regional Medical Center	Overland Park, KS, USA	Sabapathy	Rajendran	*Rajendran Sabapathy, Bangalore Deepak, George Pierson, Jayasheel Eshcol, Ujjaval Patel, Aaron Doonan,* Chelsea Waller, Elizabeth Fulks, Joyce Dahlin, Shayna Segal, Suzanne Baldwin	13
Stanford University Medical Center	Stanford, CA, USA	Tremmel	Jennifer	*David Lee, Brian Kim, William Fearon, Alan Yeung, Guson Kang, Rahul Sharma,* Daniel Kim, Gloria Han, Jaclyn Milich, Linda Mireles, Melina Demokritou, Pallavi Vaidya, Pragya Tripathi, Yasaman Nourkhalaj	12
Northside Hospital	Lawrenceville, GA, USA	Grines	Cindy	*Allison Dupont, Andrew Yen, Christopher Leach, Fredy El Sakr, Michele Voeltz, Philip Room, Pradyumna Tummala, Yuri Pride,* Kathleen Sutter, Kimberly Kelly, Nancy Bryant, Nicole Rosonina, Tamara Wakhisi	12
University of Alabama at Birmingham	Birmingham, AL, USA	Ahmed	Mustafa	*George Von Mering, Hussein Abu Daya,* Dorothy Nieters, Jane Vines, Katherine Phillips, Sarah Houston,	11
Montefiore Medical Center	Bronx, NY, USA	Latib	Azeem	*Judah Rauch, Dimitrios Bliagos, Juan Terre, Jose Wiley, Manaf Assafin, Mark Menegus, Yuhei Kobayashi,* Daniela Cabral, Mollie Machado, Nadia Soberal, Noelle Manning, Samanta Baboolall, Sheila Davila	11

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
Inova Fairfax Hospital	Falls Church, VA, USA	Tehrani	Behnam	*Kelly Epps, Alexander Truesdell, Matthew Sherwood, Nicholas Balaji, Wayne Batchelor,* Brian Moore, Diana McLean, Jean Min, Micaela Davidow, Tracy Plummer, Van Doan	10
Henry Ford Hospital	Detroit, MI, USA	Alaswad	Khaldoon	*Akshay Khandelwal, Brian O'Neill, Brittany Fuller, Mir Basir, Mohammad Alqarqaz, Mohammad Zaidan, Pedro Villablanca, Tiberio Frisoli,* Gerald Koenig, Margaret Fox, Melanee Schimmel, Pedro Villablanca Spinetto	9
Tufts Medical Center	Boston, MA, USA	Kimmelstiel	Carey	*Noah Haroian, Michael Yin, Charlie Resor, Andrew Weintraub, Michele Esposito, Mohamad El-Zaru, Navin Kapur, Aaron Lee,* Jamie Rubinstein, Paulina Baca, Richard Botto, Thayaparan Balakumar, Vilma Castaneda	9
Tallahassee Memorial Hospital	Tallahassee, FL, USA	Dixon	William	*John Katopodis, Andres Estrada, Pablo Rengifo-Moreno,* Brianna Everett, Dana Porter, Katherine Gearld, Nikki Robinson, Rebecca Plasay	9
Wellstar Kennestone Hospital	Marietta, GA, USA	Reitman	Arthur	*Abdul Sheikh, Salvatore Mannino, Frank Corrigan, III,* Jeffrey Jacob, Jennifer Cuvo, Katrina van den Brand, Michele Neese, Zamzam Kassim	9
University of California, San Diego	La Jolla, CA, USA	Ang	Lawrence	*Lawrence Ang, Belal Al Khiami, Ehtisham Mahmud, Ryan Reeves,* Bahman Ghannadian, David Wasserstein, Johnathan Omens, Lilian Von Husen, Melissa Suarez	8
Evanston Hospital	Evanston, IL, USA	Levisay	Justin	*Mark Ricciardi, Jonathan Rosenberg,* Amy Tanimoto, Bernardo Vargas, Dale Seifert, Laurene Sherman, Samantha Krause	8
Rhode Island Hospital	Providence, RI, USA	Abbott	Jinnette	*Herbert Aronow, Marwan Saad, Paul Gordon,* Catherine Gordon, Ellen Cerullo, Kelly Franchetti, Lori Ann DeSimone	8

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
University of Washington Medical Center	Seattle, WA, USA	Kearney	Kathleen	*Christine Chung, William Lombardi, Zachary Steinberg,* Adele Stefanowicz, Emma Wampler, Jennifer Schaeffer	7
Massachusetts General Hospital	Boston, MA, USA	Jaffer	Farouc	*Akl Fahed, Dahaval Kolte, Nijay Patel, Darshan Doshi, Rahul Sakhuja, Sammy Elmariah,* Chethana Venkatraman, Devin Maximus	7
Wake Medical Center	Raleigh, NC, USA	Neupane	Saroj	*France Wood,* Haleigh Berst, Justin Nalley, Rhonda Norton, Taylor Wall	6
Brigham and Women's Hospital	Boston, MA, USA	Croce	Kevin	*Brian Bergmark,* Barbora Zvarova, Mickayla Royer, Taylor Munson	6
San Francisco Veterans Affairs Medical Center	San Francisco, CA, USA	Shunk	Kendrick	*Jeffrey Zimmet, Joseph Yang,* Cynthia Huynh, Kathleen Stanley	6
University of Virginia Medical Center	Charlottesville, VA, USA	Taylor	Angela	*Kanwar Singh, Michael Ragosta, Nishta Sodhi, Lawrence Gimple,* Charlotte Pekich, Christin Henderson, Emily Guy, Linda Bryceland, Mary Knisley, Reanna Panagides, Shelly Brunk	5
Jersey Shore University Medical Center	Eatontown, NJ, USA	Saybolt	Matthew	*Daniel Kiss, Edward Choi, Matthew Schoenfeld,* Anne DeToro, Ian Taveras, Joanne Kushnir, Lynda Argenzio	4
Methodist North Hospital	Germantown, TN, USA	Diaz	Claro	*Yenel Harper, Mohamed Morsy,* Carol Jones	4
The Methodist Hospital Research Institute	Houston, TX, USA	Shah	Alpesh	*Neal Kleiman,* Adam Daniels, Aneesch Martin, Annalise Brisco, Carol Underwood, Danielle Gee, Deena Victor, Iris Alanis, Julie Marlatt, LaShawna Green, Padmaja Naik, Patricia Brinegar, Saba Khan, Tia McGaughy, Victoria Villanueva	3
Carondelet Medical Group	Tucson, AZ, USA	Lotun	Kapil	Lucy Pena, Rachael Taoka	3

Clinical Center	City, State, Country	Primary Investigator (Last Name)	Primary Investigator (First Name)	Site Staff (italicized names are Sub-Investigators)	Patients Enrolled
Regions Hospital	St. Paul, MN, USA	Brechtken	Johannes	*Amit Sharma, Lucas Christianson, Mohammad Jameel, Stephen George, William Nelson,* Allison Kehren, Aneesha Andrew, Brandon Orner, Chloe Asuncion, Corrin Thorson, David Bachman, Derek Kamal, Joshua Rosenzweig, Lucas Hale, Madelyn Blake, Michelle Orellana, Morgan MacDonald, Natasha Ahrweiler, Nathan Phan, Rebecca Floden, Wiktoria Pasek, Zuzanna Pasek	2
Bergan Cardiology	Omaha, NE, USA	Agarwal	Himanshu	*Ann Narmi, Arun Kanmantha Reddy, Khagendra Dahal, Michael Del Core, Nagarjuna Gujjula, Scott Carollo, Toufik Haddad,* Barbara Lapke, Melissa Romsa	2
Ochsner Clinic Foundation	New Orleans, LA, USA	Patel	Rajan	Cherie Bourgeois, Melanie Lunn, Michael Harrison, Monique Pellegrin, Shannon Williams	1

eTable 2. AGENT IDE Committees

Independent Data and Safety Monitoring Committee	
Name	**Institution**
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Helen Parise, ScD	Yale University School of Medicine 135 College St New Haven, CT 06510
Clinical Events Committee	
Name	**Institution**
Joseph Kannam, MD Chair	Needham Cardiology Beth Israel Deaconess - Needham 148 Chestnut Street Needham, MA 02492
Germano DiSciascio, MD	Campus Bio-Medico University of Rome Via Alvaro del Portillo 200 00128 Roma Italy
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Goran Stankovic, MD	Department of Cardiology Clinical Center of Serbia Visegradska 26, 11000 Belgrade Serbia
AGENT IDE Steering Committee	
Name	**Institution**
Robert Yeh, MD	Beth Israel Deaconess Medical Center
Ajay Kirtane, MD	Columbia University Medical Center
William Bachinsky, MD	Pinnacle Health Cardiovascular Institute
Suhail Dohad, MD	Cedars - Sinai Medical Center
Robert Stoler, MD	Baylor Heart & Vascular Hospital
Cinthia Tjan Bateman, MD	South Denver Cardiology Associates, PC
Jennifer A. Tremmel, MD, MS	Stanford University Medical Center
J. Aaron Grantham, MD	St. Luke's Hospital of Kansas City
Wayne Batchelor, MD	Inova Fairfax Hospital
Jinette Dawn Abbott, MD	Rhode Island Hospital

Study Design

Protocol and Statistical Analysis Plan (SAP)

Submitted as separate documents.

Enrollment and Study Duration

The AGENT IDE study planned an initial enrollment of at least 480 patients in up to 40 sites in the United States, with the potential for sample size re-estimation up to a maximum of 600 randomized patients if needed (see Statistical Methods). An interim analysis for the sample size re-estimation was to be performed on the 1-year data from the first 40% (192) randomized patients of the initial enrollment of 480 patients.

Clinical follow-up was required at the following time points: in-hospital, 30 days, 6 months, 1-year, and annually through 5 years post index procedure.

Patient Selection and Analysis Populations

Patients meeting all inclusion criteria and no exclusion criteria were randomized in a 2:1 allocation to either paclitaxel-coated balloon or uncoated balloon, respectively.

eTable 3. Agent IDE Study Inclusion Criteria

Clinical Inclusion Criteria	• Patient must be at least 18 years of age and eligible for PCI. • Patient (or legal guardian) understands the trial requirements and the treatment procedures and provides written informed consent before any study-specific procedures are performed. • Patient is willing to comply with all protocol requirements. • Women of child-bearing potential must agree to use a reliable method of contraception from the time of screening through 12 months after the index procedure.
Angiographic Inclusion Criteria (Visual Estimate)	• In-stent restenosis of a lesion located in a native coronary artery with RVD >2.0 mm and ≤4.0 mm, which was previously treated with a drug-eluting or bare metal stent. • Target lesion length must be <26 mm and covered by only one balloon, with stenosis >50% and <100% (symptomatic patients) or >70% and <100% (asymptomatic patients) prior to lesion pre-dilation. • Target lesion must be successfully pre-dilated*. • Up to 2 native coronary artery lesions in 2 major epicardial vessels may be treated; patients may have 1 target lesion, or 1 target lesion and 1 non-target lesion (in non-target vessel) treated. • The non-target lesion must be treated during the index procedure prior to the treatment of the target lesion and deemed an angiographic success†.

*Successful predilation/pretreatment refers to dilation with a balloon catheter of appropriate length and diameter, or pretreatment with directional or rotational coronary atherectomy, laser or cutting/scoring balloon with no greater than 50% residual stenosis and no dissection greater than National Heart, Lung, Blood Institute (NHLBI) type C, and TIMI flow in the target lesion must be >2

†Successful treatment of a non-target lesion is defined as a residual stenosis of ≤30% in 2 near-orthogonal projections with TIMI 3 flow, as visually assessed by the physician, without the occurrence of prolonged chest pain or ECG changes consistent with MI

eTable 4. Agent IDE Study Exclusion Criteria

Clinical Exclusion Criteria	• Left ventricular ejection fraction <25%. • STEMI or QWMI <72 hours prior to the index procedure. • Platelet count <100,000/mm^3 (risk of bleeding) or >700,000/mm^3. • Renal insufficiency (creatinine ≥2.0 mg/dl) or failure (dialysis dependent). • Patient presently has suspected or proven COVID-19 or within the past 4 weeks with resolution of symptoms.
Angiographic Exclusion Criteria (Visual Estimate)	• Target lesion located within saphenous vein or arterial graft, or within a bifurcation with planned treatment of a side branch vessel. • Unprotected left main coronary artery disease with >50% diameter stenosis. • Diameter stenosis of >50% in an additional lesion proximal or distal (>2.0 mm RVD) to the target lesion. • Presence of thrombus in the target vessel.

Patient Analysis Sets

All primary and additional endpoints were analyzed in an intent-to-treat (ITT) basis. All patients who signed the internal review board (IRB) approved study informed consent form (ICF) and were enrolled in the study were included in the intent-to-treat analysis according to their randomized treatment, regardless of whether or not a paclitaxel-coated balloon or an uncoated balloon was used.

Statistical Methods

Randomization

Patients were considered eligible to be enrolled in the trial after they signed the IRB approved study ICF and met all clinical inclusion and no clinical exclusion criteria. A computer-generated list of random treatment allocations (i.e., a randomization schedule) were used to assign patients to treatment in a 2:1 ratio of paclitaxel-coated balloon to uncoated balloon angioplasty. Randomization was stratified by center and single vs. multiple stent layers. Each site was allowed to enroll no more than 20% of patients of the total sample size. Investigators performing the procedure were not blinded to the assigned treatment because of different packaging of the devices. Core laboratory personnel and the clinical events committee (CEC) were blinded to a patient's treatment assignment during the trial.

Hypothesis Testing

The primary statistical hypothesis is that the rate of the primary endpoint of 1-year target lesion failure (TLF) in the paclitaxel-coated balloon group is superior to that in the uncoated balloon group. The null and alternative hypotheses for the primary endpoint are as follows:

$$H_0: TLF_{PCB} \geq TLF_{UCB}$$
$$H_1: TLF_{PCB} < TLF_{UCB}$$

where TLF_{PCB} and TLF_{UCB} correspond to the rates of 1-year TLF for the paclitaxel-coated balloon group and uncoated balloon group, respectively.

A z-test with unpooled variance for the difference of two proportions was used for testing for the primary endpoint, as described in the SAP. The primary analysis population for the primary endpoint was the ITT analysis set.

Adaptive Design and Sample Size Calculation

The statistical approach uses an adaptive group sequential design[1] with one planned formal interim analysis of the primary endpoint for the sole purpose of sample size re-estimation. The interim analysis was performed by the data and safety monitoring committee (DSMC) based on the 1-year data from the first 40% (192) of the randomized patients. As per the SAP, the study was not to be stopped early after this interim analysis; an interim alpha spending was therefore not required.

A final primary endpoint analysis with the alpha of 0.025 was performed on the final sample size from the sample size re-estimation strategy recommended by the DMSB.

The sample size calculation for the primary endpoint was based on the following assumptions:

- Expected mean TLF_{PCB} = 10.6% (based on meta-analysis of historical trials[2] and including an adjustment to account for the occulo-stenotic reflex[3])
- Expected mean TLF_{UCB} = 21.2% (based on meta-analysis of historical trials[2] and including an adjustment to account for the occulo-stenotic reflex[3])
- Test significance level (α) = 2.5% (1-sided)
- Power* = 85%
- Randomization ratio = 2 PCB: 1 UCB
- Number of evaluable patients per arm = 310 (paclitaxel-coated balloon) and 155 (uncoated balloon)
- Expected attrition rate = 3%
- Total planned enrollment = 480 patients

where TLF_{PCB} and TLF_{UCB} correspond to the rates of 1-year TLF for the paclitaxel-coated balloon group and uncoated balloon group, respectively.

*the power is the overall study power for the sample size re-estimation.

The sample size increase was limited to a maximum of 600 and the calculation was performed by using the Chen, DeMets, and Lan (CDL) method[4] such that the conventional z-test with unpooled variance for the difference of two proportions would be used for the final analysis. The sample space of the possible interim outcome was partitioned into 3 zones: unfavorable, promising, and favorable. The sample size increase was only to be performed if the conditional power (CP), defined as the probability of obtaining a positive outcome at the end of the trial, lay in the promising zone. The unfavorable zone, promising zone and favorable zone in this trial were defined as the observed conditional power at the interim analysis being less than the minimum CP (CP_{min} = 0.46), in the interval [CP_{min}, CP_{target} = 0.85] and being greater than the CP_{target} = 0.85, respectively.

AGENT IDE Endpoints

Primary Endpoint

The primary endpoint was the rate of 1-year TLF, defined as any ischemia-driven revascularization of the target lesion (TLR), myocardial infarction (MI) related to the target vessel, or cardiac death. The MI events include the periprocedural MI according to the Society for Cardiovascular Angiography and Intervention definition[5] (SCAI), and spontaneous MI occurring 48 hours after the index procedure was adjudicated according to the 4th Universal definition of MI[6].

Additional Prespecified Endpoints

Clinical endpoints:

- TLR, TLF and target vessel revascularization (TVR)
- Target vessel failure (TVF)
- MI (Q-wave and non–Q-wave); periprocedural MI per the SCAI definition[5] and spontaneous MI per the 4th Universal definition[5]
- Cardiac death
- Non-cardiac death
- All-cause death
- Stent Thrombosis (per Academic Research Consortium [ARC] definitions[7])

These endpoints were measured in hospital and at 30 days, 6 months, 12 months, then annually through 5 years. All reported events of death, MI, target vessel revascularization (TVR) and stent thrombosis (ST) were adjudicated by an independent CEC.

Periprocedural endpoint:

- Technical success was defined as successful crossing and dilation of the lesion, without balloon rupture, and post-procedure diameter stenosis of <30% in 2 near-orthogonal projections with TIMI 3 flow in the target lesion, as visually assessed by the physician.
- Clinical procedural success was defined as post-procedure diameter stenosis <30% in 2 near-orthogonal projections with TIMI 3 flow in the target lesion, as visually assessed by the physician, without the occurrence of in-hospital MI, TVR, or cardiac death.

Change in Quality of Life:

- Functional status of general health-related quality of life was measured by changes in EQ-5D scores at hospital discharge, 1-year, 2 years, and 3 years.

Supplementary Results

eTable 5. Procedural and Postprocedural Outcomes[a]

Characteristic	Paclitaxel-Coated Balloon (n = 406)	Uncoated Balloon (n = 194)	P Value
No. of Lesions	407	194	
Procedural Outcomes			
Clinical Procedural Success, no. (%)	374 (92.1)	172 (88.7)	.17
Technical Success, no./total no. (%)[b]	380/407 (93.4)	174/194 (89.7)	.12
Procedure Time, Mean (SD) (n), min	56.2 (29.8) (402)	53.2 (27.1) (193)	.23
Patients with only target lesion treated, no. (%)	355 (87.4)	168 (86.6%)	.77
Patients with both target and non-target lesion treated, no. (%)	51 (12.6%)	26 (13.4%)	.77
Intravascular imaging usage any time during procedure[b], no. (%)	294 (72.4)	149 (76.8)	.30
Bailout Stenting, no./total no. (%)	3/407 (0.7)	1/194 (0.5)	>.99
Ancillary device usage per lesion[c], no./total no. (%)			
Balloon angioplasty catheter	359/407 (88.2)	167/194 (86.1)	.46
Cutting balloon	102/407 (25.1)	46/194 (23.7)	.72
Scoring balloon	71/407 (17.4)	17/194 (8.8)	.01
Drug eluting stent	2/407 (0.5)	3/194 (1.5)	.34
Bare metal stent	0/407 (0.0)	0/194 (0.0)	Undefined
Angiographic Post-Procedural Outcomes, Mean (SD) (no.)			
Hospital length of stay[d], days	0.59 (0.93) (406)	0.72 (1.75) (194)	.24
Minimum Lumen Diameter, mm			
In-lesion[e]	2.10 (0.45) (400)	2.13 (0.49) (193)	.56

Characteristic	Paclitaxel-Coated Balloon (n = 406)	Uncoated Balloon (n = 194)	P Value
In-segment[f]	2.24 (0.45) (384)	2.28±0.49 (181)	.41
% Diameter Stenosis			
In-lesion[e]	22.64±10.30 (399)	22.47±10.32 (192)	.85
In-segment[f]	17.16±11.69 (383)	16.41±12.07 (180)	.48
Acute Gain[g], mm			
In-lesion[e]	1.15±0.45 (398)	1.22±0.50 (189)	.12
In-segment[f]	1.30±0.44 (382)	1.37±0.50 (177)	.07

All entries are n (%) or n/N (%) [when N differs from column N due to missing values], unless otherwise noted.

[a]Two-sided P values calculated with χ^2 or Fisher exact tests or t test.

[b]One patient in the DCB arm had two target lesions treated with DCB that was counted as a protocol deviation.

[c]Per lesion values (194 lesions in the uncoated balloon group and 407 lesions in the paclitaxel-coated balloon group)

[d]Site reported.

[e]In-lesion refers to treated segment.

[f]In-segment refers to total treated segment (including proximal and distal 5 mm edges to the treated segments).

[g]Acute Gain = Post-procedure MLD – Pre-procedure MLD.

eTable 6. Antiplatelet Medication Usage Through 1-Year[a]

Medication	Paclitaxel-Coated Balloon n = 406	Uncoated Balloon n = 194	P Value
	no./total no. (%)		
Aspirin			
Discharge	390/406 (96.1)	185/194 (95.4)	.69
30 Days	368/400 (92.0)	174/190 (91.6)	.86
6 Months	349/391 (89.3)	168/190 (88.4)	.76
12 Months	324/373 (86.9)	152/176 (86.4)	.87
Clopidogrel			
Discharge	269/406 (66.3)	128/194 (66.0)	.95
30 Days	269/400 (67.3)	124/190 (65.3)	.63
6 Months	252/391 (64.5)	119/190 (62.6)	.67
12 Months	237/373 (63.5)	105/176 (59.7)	.38
Ticlopidine			
Discharge	0/406 (0.0)	0/194 (0.0)	Undefined
30 Days	0/400 (0.0)	0/190 (0.0)	Undefined
6 Months	0/391 (0.0)	0/190 (0.0)	Undefined
12 Months	0/373 (0.0)	0/176 (0.0)	Undefined
Prasugrel			
Discharge	86/406 (21.2)	36/194 (18.6)	.45
30 Days	83/400 (20.8)	35/190 (18.4)	.51
6 Months	79/391 (20.2)	32/190 (16.8)	.33
12 Months	66/373 (17.7)	27/176 (15.3)	.49
Ticagrelor			
Discharge	51/406 (12.6)	33/194 (17.0)	.14
30 Days	46/400 (11.5)	30/190 (15.8)	.15
6 Months	44/391 (11.3)	28/190 (14.7)	.23

Medication	Paclitaxel-Coated Balloon n = 406	Uncoated Balloon n = 194	P Value
12 Months	38/373 (10.2)	28/176 (15.9)	.05
Clopidogrel, Ticlopidine, Prasugrel or Ticagrelor			
Discharge	404/406 (99.5)	194/194 (100.0)	>.99
30 Days	397/400 (99.3)	187/190 (98.4)	.39
6 Months	375/391 (95.9)	178/190 (93.7)	.24
12 Months	340/373 (91.2)	159/176 (90.3)	.76
Aspirin and one of Clopidogrel, Ticlopidine, Prasugrel or Ticagrelor			
Discharge	389/406 (95.8)	185/194 (95.4)	.79
30 Days	365/400 (91.3)	172/190 (90.5)	.77
6 Months	335/391 (85.7)	158/190 (83.2)	.43
12 Months	297/373 (79.6)	137/176 (77.8)	.63

All entries are n (%) or n/N (%) [when N differs from column N due to missing values], unless otherwise noted.

[a]Two-sided P values are calculated with χ^2 or Fisher exact tests.

eTable 7. One-Year Primary End Point Results in the Analysis Cohort (N=480 Patients)

	Paclitaxel-Coated balloon n = 321	Uncoated Balloon n = 159	Difference (95% CI)	One-sided 97.5% UCB	Superiority *P* Value
Target Lesion Failure, no./total no. (%)	18.2% (55/302)	29.3% (44/150)	-11.1% (-19.6% to -2.6%)	-2.6%	.0051

The primary study hypothesis pre-specified binary analyses.

The primary end point of 1-year target lesion failure is defined as the composite of ischemia-driven target lesion revascularization, target vessel-related myocardial infarction, or cardiac death.

One-sided P-value and confidence interval (CI) are from z-test with unpooled variance for the difference of two proportions.

Abbreviations: UCB, upper confidence bound.

eTable 8. Stratified Primary End Point Results (N=600 Patients)

Target Lesion Failure at 1-Year	Hazard Ratio (Paclitaxel-coated balloon vs. uncoated balloon)	95% Hazard Ratio Confidence Limits		*P* Value
Without adjustment	0.59	0.42	0.84	.0037
Adjusted by stent layer and clinical sites	0.62	0.43	0.89	.0102

Time to event analysis. P-value from Cox Regression.

The primary end point of 1-year target lesion failure is defined as the composite of ischemia-driven target lesion revascularization, target vessel-related myocardial infarction, or cardiac death.

eTable 9. Competing Risk Analysis for the Primary Endpoint (N=600)

Target Lesion Failure at 1-Year	Paclitaxel-coated balloon (n=406)	Uncoated balloon (n=194)	*P* Value
Cumulative Incidence Function	17.9% (14.3%, 21.8%)	28.5% (22.2%, 35.1%)	.004

Primary endpoint results based on the cumulative incidence function to account for the competing risk of non-cardiac death.

P-value from Gray's test.

The primary end point of 1-year target lesion failure is defined as the composite of ischemia-driven target lesion revascularization, target vessel-related myocardial infarction, or cardiac death.

eTable 10. EQ-5D Scores Through 1-Year[a]

Measure	Paclitaxel-Coated Balloon n = 426	Uncoated Balloon N = 194	*P* Value
	Mean (SD) (n)		
Baseline			
EQ-5D Index Score Summary	0.83 (0.15) (404)	0.82 (0.15) (194)	.37
EQ-5D VAS Score Summary	68.68 (19.12) (404)	69.82 (19.36) (194)	.49
Discharge			
EQ-5D Index Score Summary	0.87 (0.15) (400)	0.85 (0.16) (192)	.22
% Change from Baseline	7.08 (27.74) (398)	5.66 (22.44) (192)	.54
EQ-5D VAS Score Summary	75.47 (18.82) (400)	74.53 (19.48) (192)	.57
% Change from Baseline	13.67 (34.51) (398)	11.25 (34.58) (191)	.43
12 Months			
EQ-5D Index Score Summary	0.86 (0.15) (363)	0.84 (0.19) (172)	.22
% Change from Baseline	5.07 (23.81) (361)	3.08 (30.65) (172)	.41
EQ-5D VAS Score Summary	75.45 (16.66) (363)	73.40 (18.04) (172)	.19
% Change from Baseline	23.39 (121.90) (361)	13.56 (56.11) (171)	.32

[a]Two-sided P values are calculated with t test.

Abbreviation: VAS, visual analog scale

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