Five-Year Clinical Outcomes After Coronary Bioresorbable Scaffolds and Drug-Eluting Stents: The ABSORB IV Randomized Trial

Gregg W. Stone, MD, Dean J. Kereiakes, MD, Tommaso Gori, MD, D. Christopher Metzger, MD, Bernardo Stein, MD, Matthew Erickson, MD, Jan Torzewski, MD, Ameer Kabour, MD, Guy Piegari, MD, Jeffrey Cavendish, MD, Barry Bertolet, MD, Kelly A. Stockelman, PhD, Nick E.J. West, MD, Ori Ben-Yehuda, MD, James W. Choi, MD, Steven O. Marx, MD, John A. Spertus, MD, MPH, Stephen G. Ellis, MD, for the ABSORB IV Investigators

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Gregg W. Stone, MD, Dean J. Kereiakes, MD, Stephen G. Ellis, MD, for the ABSORB IV Investigators

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ABSORB IV study organization and sites

Principal Investigator and Study Chairman: Gregg W. Stone, The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, New York, NY, USA

Co-Principal Investigators: Stephen G. Ellis, Cleveland Clinic, Cleveland OH; Dean J. Kereiakes, The Christ Hospital, Cincinnati, OH, USA

Steering Committee: Gregg W. Stone, The Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY, USA; Stephen G. Ellis, Cleveland Clinic, Cleveland, OH, USA; Dean J. Kereiakes, The Christ Hospital, Cincinnati, OH, USA

Clinical Events Committee: The Cardiovascular Research Foundation, New York, NY, USA: Steven Marx (Chair), Ozgen Dogan (Co-Chair), Clive Rosendorff (Co-Chair), David Engel, Stanley Schneller, Arash Salemi, Geoffrey Pitt, Kevin G Dunsky.

Clinical Events Committee for Angina Questionnaire: The Cardiovascular Research Foundation, New York, NY, USA: Saif Anwaruddin, James Coromilas, Nicola Corvaja, Frederick Feit, Kirk Garratt, Newsha Z. Ghodsi, Mun K. Hong, Christian Schulze, Daichi Shimbo, Alejandro Torres, Torsten P. Vahl.

Angiographic Core Laboratory Analysis: The Cardiovascular Research Foundation, New York, NY, USA: Ziad A. Ali (Director), Ivana Jankovic (Director), Mitchel B. Lustre (Assistant Director), Philippe Généreux (Former Director).

Cost-effectiveness and Quality of Life Assessment: Health Economics and Technology Assessment Group, Saint Luke's Mid America Heart Institute, Kansas City, MO, USA: David J.

Cohen, Elizabeth Magnuson, Suzanne J. Baron, Suzanne V. Arnold, Kaijun Wang, Kate Vilain, Kendra Traylor.

Patient Perception Data Collection: Saint Luke's Mid America Heart Institute, Kansas City, MO, USA: John Spertus (Director), Kensey Gosch, Marci Kennedy.

Patient Perception Data Analysis: Pharmtrials Consultants Inc., Raleigh, NC, USA.

Digital Imaging and Communications in Medicine (DICOM) Image Archival and Transfer of Angiograms, IVUS and OCT: Bioclinica, Inc, Princeton, NJ, USA

Interactive Voice Response System (IVRS) support: Bracket Global LLC, San Francisco, CA, USA.

Data Management: Abbott Vascular, Santa Clara, CA, USA.

Biostatistics and Data Analysis: Abbott Vascular, Santa Clara, CA, USA.

Data Safety Monitoring Board (DSMB): Axio Research, Seattle, WA, USA: Robert N. Piana, Richard Milani, Carey Kimmelstiel, Bruce C. Stouch.

Sponsor and funding: Abbott Vascular, Santa Clara, CA, USA.

Participating countries, hospitals, and principal investigators:

United States (2062 randomized): Ballad Health Systems CVA Heart Institute, Kingsport, TN: Christopher Metzger; Morton Plant Hospital, Clearwater, FL: Patrick Cambier, Bernardo Stein; Presbyterian Hospital, Charlotte, NC: Jerome Williams; Stony Brook University Medical Center, Stony Brook, NY: Luis Gruberg; The Christ Hospital, Cincinnati, OH: Thomas Broderick; Mercy St. Vincent Medical Center, Toledo, OH: Ameer Kabour; St. Joseph Medical Center, Wyomissing, PA: Guy Piegari; Scripps Memorial Hospital La Jolla, La Jolla, CA: Richard Fortuna, Jeffrey Cavendish; North Mississippi Medical Center, Tupelo, MS: Barry Bertolet; Baylor Jack and Jane Hamilton Heart and Vascular Hospital, Dallas, TX: James Choi;

MedSTAR Washington Hospital Center, Hyattsville, MD: Ron Waksman, Lowell Satler; Winchester Medical Center, Winchester, VA: Neal Gaither; Rex Hospital, Inc., Raleigh, NC: James Zidar; MedSTAR Union Memorial Hospital, Hyattsville, MD: John Wang; Baptist Medical Center, Jacksonville, FL: Marc Litt; St. Joseph's Hospital Health Center, Liverpool, NY: Ronald Caputo; Medical Center of the Rockies, Loveland, CO: Anthony Doing; AnMed Health, Anderson, SC: Brent McLaurin; Northwest Texas Healthcare System, Amarillo, TX: Joaquin Martinez-Arraras; Washington Hospital, Fremont, CA: Ash Jain; Seton Medical Center, Austin, TX: Osvaldo Gigliotti; Sharp Memorial Hospital, San Diego, CA: John Gordon; Chandler Regional Medical Center, Gilbert, AZ: Nabil Dib; Jewish Hospital, Louisville, KY: Naresh Solankhi; St. Joseph Mercy Hospital, Ypsilanti, MI: Herbert Aronow, Zakir Sahul; East Texas Medical Center, Tyler, TX: Robert Carney; Holy Spirit Hospital, Camp Hill, PA: Rajesh Dave; Geisinger Medical Center, Danville, PA: Kimberly Skelding; Our Lady of Lourdes Medical Center, Haddon Heights, NJ: Vijayendra Verma, Audrey Sernyak; Northern Michigan Hospital, Petoskey, MI: Louis Cannon; The Ohio State University Medical Center, Columbus, OH: Vincent Pompili, Konstantinos Boudoulas; Mercy Hospital Springfield, Springfield, MO: Robert Merritt; UF Health Jacksonville, Jacksonville, FL: Theodore Bass; Doylestown Hospital, Doylestown, PA: Steven Guidera: University of Kentucky Hospital, Lexington, KY: Khaled Ziada; Mary Hitchcock Memorial Hospital, Lebanon, NH: Aaron Kaplan; Mount Sinai Medical Center, New York, NY: Annapoorna Kini, Samin Sharma; Pinnacle Health at Harrisburg Hospital, Wormleysburg, PA: William Bachinsky; Emory University Hospital, Atlanta, GA: Habib Samady; St. John's Hospital, Springfield, IL: Gregory Mishkel, Shailesh Nandish; Eastern Maine Medical Center, Bangor, ME: Peter Ver Lee; NYP Weill Cornell Medical Center, New York, NY: Shing Wong; Tallahassee Memorial Hospital, Tallahassee, FL: Wayne Batchelor;

Integris Baptist Medical Center, Inc., Oklahoma City, OK: George Chrysant; Little Company of Mary Hospital, Torrance, CA: Michele Vicario; University of Alabama at Birmingham, Birmingham, AL: Massoud Leesar; Columbia University Medical Center, New York, NY: Jeffrey Moses; Boone Hospital Center, Columbia, MO: Anthony Spaedy; Providence Hospital, Columbia, SC: Patrick. Hall, Michael Foster; St. John Hospital & Medical Center, Detroit, MI: Thomas Davis, Hiroshi Yamasaki; New York Hospital Queens, Flushing, NY: Chong Park; Carolinas Medical Center, Charlotte, NC: Bryan Wilson; UPMC Presbyterian Hospital, Pittsburgh, PA: Catalin Toma; Arkansas Heart Hospital, Little Rock, AR: David Mego; Elkhart General Hospital, Elkhart, IN: Donald Westerhausen; University of Massachusetts Memorial Medical Center, Worcester, MA: Jeffrey Rade; Harper University Hospital, Detroit, MI: Theodore Schreiber; Cooper University Hospital, Heights, NJ: Georges Kaddissi; Scottsdale Healthcare, Scottsdale, AZ: David Rizik; John Muir Health Concord, Concord, CA: Gary Gershony; Stanford Hospital and Clinics, Stanford, CA: Alan Yeung; Northwestern Memorial Hospital, Chicago, IL: Mark Ricciardi, Charles Davidson; University of California Davis Medical Center, Sacramento, CA: Reginald Low; WakeMed, Raleigh, NC: William Newman, Pratik Desai; Nebraska Heart Institute Heart Hospital, Lincoln, NE: Douglas Netz; Ochsner Clinic Foundation, New Orleans, LA: Rajan Patel, J. Stephen Jenkins; St. Patrick Hospital, Missoula, MT: Mark Sanz, James Maddux; Rochester General Hospital, Rochester, NY: Thomas Stuver, Gerald Gacioch; Yale-New Haven Hospital, New Haven, CT: Michael Cleman, Robert Attaran; Baptist Health Lexington, Lexington, KY: Michael Jones; Carilion Roanoke Memorial Hospital, Roanoke, VA: Timothy Ball, Gary Swank; The Methodist Hospital, Research Institute, Houston, TX: Alpesh Shah; Englewood Hospital and Medical Center, Englewood, NJ: Joseph DeGregorio; Boston Medical Center, Boston, MA: Alice Jacobs; Strong Memorial Hospital,

Rochester, NY: Frederick Ling; Providence St. Vincent Medical Center, Portland, OR: Ethan Korngold; Vanderbilt University Medical Center, Nashville, TN: John McPherson, Mark Glazer: Holy Cross Hospital, Fort Lauderdale, FL: Joshua Purow; The Miriam Hospital plus Rhode Island Hospital, Providence, RI: Paul Gordon; Franciscan St. Francis Health, Indianapolis, IN: Saeed Shaikh, William Berg; William Beaumont Hospital, Royal Oak, MI: Amr Abbas, Simon Dixon; Cleveland Clinic, Cleveland, OH: Russel Raymond; Providence Everett Med Center, Everett, WA: Mahesh Mulumudi; Penn Presbyterian Medical Center, Philadelphia, PA: Gene Chang; Allegheny General Hospital, Pittsburgh, PA: Tony Farah; Cedars Sinai Medical Center, Los Angeles, CA: Raj Makkar, Mamoo Nakamura; Good Samaritan Medical Center, Zanesville, OH: Abdulhay Albirini; Tampa General Hospital, Tampa, FL: Fadi Matar; Aultman Hospital, Canton, OH: John Paulowski; Memorial Regional Hospital, Hollywood, FL: Luis Tami; Sanford USD Medical Center, North Sioux Falls, SD: Tomasz Stys; Banner Heart Hospital, Mesa, AZ: Alphonse Ambrosia; Loyola University Medical Center, Chicago, IL: Ferdinand Leya; Montefiore Medical Center, Bronx, NY; Vankeepuram Srinivas, Anna Bortnick; Barnes Jewish Hospital, St. Louis, MO: Jasvindar Singh; Advocate Christ Medical Center, Oak Lawn, IL: Paul Silverman; St. Luke's Episcopal Hospital, Houston, TX: Emersonerin; Bergan Mercy Medical Center, Omaha, NE: Himanshu Agarwal; Oakwood Hospital and Medical Center, Dearborn, MI: Samir Dabbous; St. Vincent Heart Center of Indiana, Indianapolis, IN: James Hermiller; Torrance Memorial Medical Center, Torrance, CA: Ray Wyman; Jersey Shore University Medical Center, Neptune, NJ : Matthew Bach; Wake Forest University Baptist Medical Center, Winston-Salem, NC: Robert Applegate; Greenville Memorial Hospital, Greenville, SC: Jesse Jorgensen; Bay Regional Medical Center, Bay City, MI: Daniel Lee; Baptist Health Louisville, Louisville, KY: Thomas Tu; Texas Health Harris Methodist, Fort Worth, TX: Gurpreet Baweja;

Memorial Hospital, Chattanooga, TN: Brian Negus; Maine Medical Center, Portland, ME: Thomas Ryan; Sutter Memorial Hospital, Sacramento, CA: David Roberts; Palm Beach Gardens Medical Center, Gardens, FL: Augusto Villa, Neerav Shah; Good Samaritan Hospital, Los Angeles, CA: Steven Burstein; Rhode Island Hospital, Providence, RI: Barry Sharaf, Jinnette Abbott; St. Vincents Medical Center, Jacksonville, FL: Samer Garas; Bryn Mawr Hospital, Bryn Mawr, PA: Antonis Pratsos; Morristown Medical Hospital, Morristown, NJ: Barry Cohen; Piedmont Hospital Atlanta, Atlanta, GA: David Kandzari; Northeast Georgia Medical Center, Gainesville, GA: John Marshall; Sacred Heart Medical Center, Springfield, OR: Dennis Gory.

Australia (148 randomized): Royal Perth Hospital, WA, Australia: Matthew Erickson; St. Vincent's Hospital Melbourne, VIC, Australia: Robert Whitbourn; Liverpool Hospital, NSW, Australia: Craig Juergens; The Prince Charles Hospital, QLD, Australia: Darren Walters; Royal Brisbane and Women's Hospital, QLD, Australia: Peter Stewart.

Germany (335 randomized): Johannes Gutenberg- Universitaet Langenbeckstr, Mainz, Germany: Tommaso Gori; Kliniken Oberallgäu GmbH, Immenstadt, Germany: Jan Torzewski; Universitätsklinik um Ulm ALBERT- EINSTEIN, Ulm, Germany: Jochen Wöhrle; Universitätsklinik um Giessen und Marbug, Giessen, Germany: Holger Nef; Segeberger Kliniken GmbH, Bad Segeberg, Germany: Ralph Tölg, Mohammed Abdel-Wahab; Elisabeth-Krankenhaus, Essen, Germany: Christoph Naber; Immanuel Klinikum, Bernau, Germany: Christian Butter; Universitätsklinik um Bonn, Bonn, Germany: Nikos Werner; Klinikum Oldenburg, Oldenburg, Germany: Albrecht Elsässer; Universitätsklinik um Freiburg, Freiburg, Germany: Constantin von Zur Mühlen.

Singapore (5 randomized): National Heart Center Singapore, Singapore: Tian Hai Koh.

Canada (54 randomized): CHUM-Hotel Dieu, Qc, Canada: André Kokis; Hôpital du Sacré-Coeur, PQ, Canada: Eric Schampaert; Montreal Heart Institute, Qc, Canada: Jean Francois Tanguay; St. Michael's Hospital, ON, Canada: Christopher Buller.

Table S1. Patient inclusion and exclusion criteria for the ABSORB IV trial

Inclusion Criteria (all must be present)
I. General Inclusion Criteria
1. Subject must be at least 18 years of age.
2. Subject or a legally authorized representative must provide written Informed Consent prior to any study related procedure, per site requirements.
3. Subject must have evidence of myocardial ischemia (e.g., silent ischemia, stable or unstable angina, non-ST-segment elevation MI (NSTEMI), OR recent ST-segment elevation MI (STEMI). Patients with stable coronary syndromes can be enrolled any time after symptom onset if eligibility criteria are otherwise met. Patients with acute coronary syndrome can be enrolled under the following conditions: a. Unstable angina or NSTEMI within 2 weeks of the index procedure. b. STEMI >72 hours ≤2 weeks prior to the index procedure. Note: Subjects with UA or NSTEMI or STEMI occurring >2 weeks of the index procedure can be included in the trial but should be categorized based on their current angina class.
4. Subjects must be suitable for PCI. Subjects with stable angina or silent ischemia and <70% diameter stenosis must have objective signs of ischemia as determined by one of the following: abnormal stress echocardiogram, nuclear scan, ECG, PET, MRI, and/or fractional flow reserve (FFR). (Note: subject with silent ischemia must have a prior history of typical angina, angina-equivalent symptoms, or atypical angina within the past year to be included in the trial.)
5. Subject must be an acceptable candidate for coronary artery bypass graft (CABG) surgery.
6. Female subject of childbearing potential who does not plan pregnancy for up to 1 year following the index procedure. For a female subject of childbearing potential a pregnancy test must be performed with negative results known within 7 days prior to the index procedure per site standard.
7. Female subject is not breast-feeding at the time of the screening. visit and will not be breast-feeding for at least 1 year following the index procedure.
8. Subject agrees to not participate in any other investigational or invasive clinical study for a period of 5 years following the index procedure.
II. Angiographic Inclusion Criteria
1. Treatment of up to three *de novo* lesions in a maximum of two epicardial vessels, with a maximum of two lesions per epicardial vessel. If only a single lesion is to be treated,

it must be a target lesion. Up to one non-target lesion can be treated. Non-target lesion treatment can occur only in a non-target vessel. If there are two target lesions within the same epicardial vessel, the two target lesions must be at least 15 mm apart per visual estimation; otherwise this is considered as a single target lesion for lesion (and stent) length determination and must be treated with a single study device.
2. Target lesion(s) must be located in a native coronary artery with a visually estimated or quantitatively assessed %DS of ≥50% and <100%, with a TIMI flow of ≥1, and one of the following: stenosis ≥70%, an abnormal functional test (e.g., fractional flow reserve ≤0.80 AND/OR a positive stress test), or presentation with an acute coronary syndrome (unstable angina or NSTEMI within 2 weeks of index procedure, or STEMI >72 hours but ≤2 weeks prior to the index procedure). Note: Subjects with UA or NSTEMI or STEMI occurring >2 weeks of the index procedure can be included in the trial but should be categorized based on their current angina class.
3. Target lesion(s) must be located in a native coronary artery with RVD by visual estimation of ≥2.50 mm and ≤3.75 mm. Note: To exclude enrollment of excessively small vessels, if the operator believes that based on visual angiographic assessments, the distal reference vessel diameter is ≤2.75 mm such that the plan is to implant a 2.5 mm device (stent or scaffold) in a target lesion, it is strongly recommended that either on-line QCA or intravascular imaging (ultrasound or optical coherence tomography) is used and demonstrates that the measured distal RVD for this target lesion is ≥2.50 mm (by at least one of these imaging modalities). This measurement may be performed before or after pre-dilatation, but before randomization. If the distal RVD measures <2.5 mm, that lesion IS NOT ELIGIBLE for randomization. Such a lesion may be treated as a non-target lesion.
4. Target lesion(s) must be located in a native coronary artery with length by visual estimation of ≤24 mm.
Exclusion Criteria (all must be absent)
I. General Exclusion Criteria
1. Any surgery requiring general anesthesia or discontinuation of aspirin and/or a P2Y12 receptor inhibitor is planned within 12 months after the procedure.
2. Subject has known hypersensitivity or contraindication to device material and its degradants (everolimus, poly(L-lactide), poly(DL-lactide), lactide, lactic acid) and cobalt, chromium, nickel, platinum, tungsten, acrylic and fluoropolymers that cannot be adequately pre-medicated. Subject has a known contrast sensitivity that cannot be adequately pre-medicated.
3. Subject has known allergic reaction, hypersensitivity or contraindication to any of the following: aspirin; or clopidogrel and prasugrel and ticagrelor; or heparin and bivalirudin, and therefore cannot be adequately treated with study medications.
4. Subject had an acute STEMI (appropriate clinical syndrome with ≥1 mm of ST-segment elevation in ≥2 contiguous leads) within 72 hours of the index procedure.

5. Subject has a cardiac arrhythmia identified at the time of screening for which at least one of the following criteria is met: a. Subject requires coumadin or any other agent for chronic oral anticoagulation. b. Subject is likely to become hemodynamically unstable due to their arrhythmia. c. Subject has poor survival prognosis due to their arrhythmia.
6. Subject has a left ventricular ejection fraction (LVEF) <30% assessed by any quantitative method, including but not limited to echocardiography, MRI, multiple-gated acquisition (MUGA) scan, contrast left ventriculography, PET scan, etc. LVEF may be obtained within 6 months prior to the procedure for subjects with stable CAD. For subjects presenting with ACS, LVEF must be assessed within 1 week of the index procedure and after ACS presentation, which may include contrast left ventriculography during the index procedure but prior to randomization in order to confirm the subject's eligibility.
7. Subject has undergone prior PCI within the target vessel during the last 12 months. Prior PCI within the non-target vessel or any peripheral intervention is acceptable if performed anytime >30 days before the index procedure, or between a minimum of 24 hours and 30 days before the index procedure if successful and uncomplicated.
8. Subject requires future staged PCI of any lesion other than a target lesion identified at the time of index procedure; or subject requires future peripheral vascular interventions < 30 days after the index procedure.
9. Subject has received any solid organ transplants or is on a waiting list for any solid organ transplants.
10. At the time of screening, the subject has a malignancy that is not in remission.
11. Subject is receiving immunosuppressant therapy or has known immunosuppressive or severe autoimmune disease that requires chronic immunosuppressive therapy (e.g., human immunodeficiency virus, systemic lupus erythematosus, etc.). Note: corticosteroids are not included as immunosuppressant therapy.
12. Subject has previously received or is scheduled to receive radiotherapy to a coronary artery (vascular brachytherapy), or the chest/mediastinum.
13. Subject is receiving or will require chronic anticoagulation therapy (e.g., coumadin, dabigatran, apixaban, rivaroxaban, edoxaban or any other related agent for any reason).
14. Subject has a platelet count <100,000 cells/mm^3 or >700,000 cells/mm^3.
15. Subject has a documented or suspected hepatic disorder as defined as cirrhosis or Child-Pugh ≥ Class B.
16. Subject has renal insufficiency as defined as an estimated GFR <30 ml/min/1.73m^2 or dialysis at the time of screening.
17. Subject is high risk of bleeding for any reason; has a history of bleeding diathesis or coagulopathy; has had a significant gastrointestinal or significant urinary bleed within the past six months.
18. Subject has had a cerebrovascular accident or transient ischemic neurological attack (TIA) within the past six months, or any prior intracranial bleed, or any permanent

neurologic defect, or any known intracranial pathology (e.g. aneurysm, arteriovenous malformation, etc.).
19. Subject has extensive peripheral vascular disease that precludes safe 6 French sheath insertion. Note: femoral arterial disease does not exclude the patient if radial access may be used.
20. Subject has a life expectancy <5 years for any non-cardiac or cardiac cause.
21. Subject is in the opinion of the Investigator or designee, unable to comply with the requirements of the study protocol or is unsuitable for the study for any reason. This includes completion of Patient Reported Outcome instruments.
22. Subject is currently participating in another clinical trial that has not yet completed its primary endpoint.
23. Subject is part of a vulnerable population who, in the judgment of the investigator, is unable to give Informed Consent for reasons of incapacity, immaturity, adverse personal circumstances or lack of autonomy. This may include: Individuals with a mental disability, persons in nursing homes, children, impoverished persons, persons in emergency situations, homeless persons, nomads, refugees, and those incapable of giving informed consent. Vulnerable populations also may include members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the Sponsor, members of the armed forces, and persons kept in detention.
II. Angiographic Exclusion Criteria All exclusion criteria apply to the target lesion(s) or target vessel(s).
1. Unsuccessful pre-dilatation, defined as the presence of one or more of the following (note: successful pre-dilatation of at least one target lesion is required prior to randomization): a. Residual %DS after pre-dilatation is ≥ 40% (per visual estimation). Note: achieving a %DS ≤ 20% prior to randomization is strongly recommended. b. TIMI flow grade <3 (per visual estimation). c. Any angiographic complication (e.g. distal embolization, side branch closure). d. Any dissection NHLBI grade D-F. e. Any chest pain lasting > 5 minutes. f. Any ST-segment depression or elevation lasting > 5 minutes.
2. Lesion is located in left main or there is a ≥30% diameter stenosis in the left main (unless the left main lesion is a protected left main (i.e. a patent bypass graft to the LAD and/or LCX arteries is present), and there is no intention to treat the protected left main lesion).
3. Aorto-ostial RCA lesion (within 3 mm of the ostium).
4. Lesion located within 3 mm of the origin of the LAD or LCX.
5. Lesion involving a bifurcation with a a) side branch ≥2 mm in diameter, or b) side branch with either an ostial or non-ostial lesion with diameter stenosis >50%, or c) side branch requiring dilatation.

6. Anatomy proximal to or within the lesion that may impair delivery of the Absorb BVS or XIENCE stent: a. Extreme angulation (≥ 90°) proximal to or within the target lesion. b. Excessive tortuosity (≥ two 45° angles) proximal to or within the target lesion. c. Moderate or heavy calcification proximal to or within the target lesion. If IVUS used, subject must be excluded if calcium arc in the vessel prior to the lesion or within the lesion is ≥180°.
7. Lesion or vessel involves a myocardial bridge.
8. Vessel has been previously treated with a stent and the target lesion is within 5 mm proximal or distal to a previously stented lesion.
9. Target lesion located within an arterial or saphenous vein graft or distal to any arterial or saphenous vein graft.

Reprinted with minor revisions from Stone GW, Ellis SG, Gori T, et al. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. Lancet. 2018;392:1530-1540.

Table S2. Primary and secondary endpoints for the ABSORB IV trial

Primary endpoint
TLF through 30 days, tested for non-inferiority of Absorb BVS against the control
Powered secondary endpoints
1. TLF through 1 year, tested for non-inferiority of Absorb BVS against the control 2. The percentage of patients who experienced angina within 1 year, tested first for non-inferiority of Absorb BVS against the control, with reflex to superiority if noninferiority is met
Additional secondary endpoints
Acute Success - Device success (lesion level analysis) - Procedural success (patient level analysis) **Clinical Endpoints** (assessed in-hospital and at 30 days, 90 days, 180 days, 270 days and at 1 year, and then annually for at least 5 years and at most 10 years.*) <u>Component endpoints</u> Death - Cardiac - Vascular - Non-cardiovascular Myocardial Infarction - Attributable to target vessel (TV-MI) - Not attributable to target vessel (NTV-MI) Target Lesion Revascularization (TLR) - Ischemia-driven TLR (ID-TLR) - Non-ID-TLR (NID-TLR) Target Vessel Revascularization (TVR) - ID-TVR - Non-ID-TVR

All coronary revascularization

Composite Endpoints

- Death/All MI
- Cardiac Death/All MI
- Cardiac Death/TV-MI/ID-TLR (TLF)
- Cardiac Death/All MI/ID-TLR (MACE)
- Cardiac Death/All MI//ID-TVR (TVF)
- Death/All MI/All revascularization (PoCE)

Scaffold/Stent Thrombosis

- Evidence (definite, probable, definite or probable)
- Timing (acute, sub-acute, late and very late)

Rehospitalization

- Coronary artery disease related
- Cardiovascular, non-CAD related
- Non-cardiovascular related

Repeat coronary arteriography

Landmark analyses*

- 30d-1 year/1-2/2-3/3-4/3-5 years for TLF and components
- 30d-1 year/1-2/2-3/3-4/3-5 years for MACE and TVF and their components
- 30d-1 year/1-2/2-3/3-4/3-5 years for scaffold/stent thrombosis

*Patients were consented for up to 10-year follow-up. Follow-up in the present trial was concluded after 5 years. CAD, coronary artery disease; ID, ischemia-driven; MACE, major adverse cardiovascular events; MI, myocardial infarction; PoCE, patient oriented composite endpoint; TLF, target lesion failure; TLR, target lesion revascularization; TV, target vessel; TVF, target vessel failure; TVR, target vessel revascularization. Modified from Stone GW, Ellis SG, Gori T, et al. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. Lancet. 2018;392:1530-1540.

Table S3. Definitions of the major endpoints for the ABSORB IV trial

Acute Success	
Device success (lesion level)	Successful delivery and deployment of study scaffold/stent at intended target lesion, and successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA)
Procedural success (patient level)	Successful delivery and deployment of at least one study scaffold/stent at intended target lesion, and successful withdrawal of delivery system and final in-scaffold/stent DS <30% (QCA), and no in-hospital (maximum 7 days) TLF
Angina	
Any angina or angina equivalent symptoms determined by the physician and/or research coordinator after interview of the patient, and as adjudicated by the clinical events committee (CEC). This endpoint will exclude angina or angina equivalent symptoms that occurred following the index procedure through hospital discharge or 7 days, whichever occurs first.	
Death	
Cardiac	Any death due to proximate cardiac cause (e.g. MI, low-output failure, fatal arrhythmia), unwitnessed death and death of unknown cause, all procedure related deaths including those related to concomitant treatment. Note: All deaths are considered cardiac unless an unequivocal non-cardiac cause can be established. Specifically, any unexpected death even in patients with coexisting potentially fatal non-cardiac disease (e.g. cancer, infection) are classified as cardiac.
Vascular	Death due to non-coronary vascular causes such as cerebrovascular disease, pulmonary embolism, ruptured aortic aneurysm, dissecting aneurysm, or other vascular cause.
Non-cardiovascular	Any death not covered by the above definitions, such as death caused by infection, malignancy, sepsis, pulmonary causes, accident, suicide or trauma.
Myocardial infarction[1]	

Periprocedural MI (within 48 hours after a revascularization procedure)*	
1. Patients with a) stable CAD, or b) silent ischemia, or c) acute coronary syndromes with at least 2 baseline troponin values which remained <ULN, or d) acute coronary syndromes in whom the troponin and/or CK-MB levels were elevated but all returned to <ULN prior to the procedure	Absolute CK-MB rises within 48 hours of the procedure to >5x ULN for post-PCI or CK-MB >10x ULN for post-CABG[2,3]
2. Patients with stable CAD and elevated baseline CK-MB, or acute coronary syndromes in whom at least 2 baseline troponin and CK-MB values were drawn and the most recent troponin and CK-MB values were less than the preceding measures by >25%	Absolute incremental CK-MB rise within 48 hours of the procedure from the most recent CK-MB level by >5x ULN for post-PCI or >10x ULN for post-CABG
3. Patients with elevated baseline CK-MB in whom the biomarker levels have not been shown to be stable or falling as defined above (either because only one CK-MB was measured, or the most recent CK-MB measure in a series was either still increasing or had not decreased by >25% from the most recent measure)	The CK-MB rises within 48 hours of the procedure by an absolute increment from the most recent CK-MB level of >5x ULN for post-PCI or >10x ULN for post-CABG plus new ST-segment elevation or depression plus signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension Plus The following must also be present: 1. New ST-segment elevation or depression, and 2. Signs consistent with a clinically relevant MI, such as new onset or worsening heart failure or sustained hypotension.
Spontaneous MI (before or >48 hours after any coronary revascularization procedure)	Troponin >ULN or CK-MB >ULN Plus One or more of the following must also be present: - Symptoms of ischemia; - ECG changes indicative of new ischemia - (new ST-T changes or new LBBB), - Development of pathological Q waves;

	- Imaging evidence of a new loss of viable myocardium or a new regional wall motion abnormality
Q-wave MI	Development of new, pathological Q waves on the ECG (≥0.04 seconds in duration and ≥1 mm in depth) in ≥2 contiguous precordial leads or ≥2 adjacent limb leads)
Non-Q-wave MI	All MIs which are not Q-wave MIs
Target vessel-related MI	MIs adjudicated to the epicardial coronary artery containing the target lesion on the basis of electrocardiographic, imaging or angiographic findings; MIs which cannot be definitely adjudicated to a non-target vessel are considered target vessel-related MI
Non-target vessel-related MI	All MIs which are not target vessel-related MIs
Revascularization	
Target lesion revascularization	Any repeat percutaneous intervention of the target lesion or bypass surgery of the target vessel performed for restenosis or other complication of the target lesion. All TLR should be classified prospectively as ischemia-driven or not ischemia-driven by the investigator prior to repeat angiography. An independent angiographic core laboratory should verify that the severity of percent diameter stenosis meets requirements for clinical indication and will overrule in cases where investigator reports are not in agreement. The target lesion is defined as the treated segment from 5 mm proximal to the stent and to 5 mm distal to the stent.
Non-target lesion target vessel revascularization	Any revascularization in the target vessel for a lesion other than the target lesion (includes all of the branches of the epicardial coronary artery containing the target lesion)
Target vessel revascularization	TLR or Non-TLR TVR
Non-target vessel revascularization	Revascularization of any vessel not containing a target lesion at the time of the index procedure. This vessel may or may not

	have been treated previously with a non-study device.
Any revascularization	Any TVR or Non-TVR, whether by PCI or CABG
Ischemia-driven revascularization	A revascularization is considered ischemia-driven if associated with any of the following: 1) Positive functional ischemia study including positive FFR; or 2) Ischemic symptoms and angiographic diameter stenosis ≥50% by core laboratory QCA; or 3) Angiographic diameter stenosis ≥70% by core laboratory QCA without angina or a positive functional study.
Non-ischemia-driven revascularization	A revascularization which is not ischemia-driven.
Stent or Scaffold Thrombosis[4]	
Protocol definition of device thrombosis	Definite or probable
Definite device thrombosis	Requires angiographic or pathologic confirmation. Angiographic confirmation of stent/scaffold thrombosis is defined as the presence of a thrombus that originates in the stent/scaffold or in the segment 5 mm proximal or distal to the stent/scaffold, with at least 1 of the following criteria within a 48-hour time window: 1) acute onset of ischemic symptoms at rest; 2) new ischemic ECG changes that suggest acute ischemia; 3) typical rise and fall in cardiac biomarkers (refer to definition of spontaneous MI); 4) nonocclusive thrombosis (a spheric, ovoid, or irregular noncalcified filling defect or lucency surrounded by contrast material on 3 sides or within a coronary stenosis seen in multiple projections, or persistence of contrast material within the lumen), or a visible embolization of intraluminal material downstream; 5) occlusive thrombus (TIMI 0 or TIMI 1 intrastent/scaffold or proximal to a stent/scaffold up to the most adjacent

	proximal side branch or main branch (if originates from the side branch). Pathological confirmation of stent/scaffold thrombosis is defined as evidence of recent thrombus within the stent/scaffold determined at autopsy or via examination of tissue retrieved following thrombectomy. Note: The incidental angiographic documentation of stent/scaffold occlusion in the absence of clinical signs or symptoms is not considered a confirmed stent/scaffold thrombosis (silent occlusion).
Probable device thrombosis	1) any unexplained death within the first 30 days after intracoronary stent/scaffold implantation (note: for patients presenting with STEMI, one may consider the exclusion of unexplained death within 30 days as evidence of probable stent thrombosis); OR 2) irrespective of the time after the index procedure, any MI that is related to documented acute ischemia in the territory of the implanted stent/scaffold without angiographic confirmation of stent/scaffold thrombosis and in the absence of any other obvious cause
Acute device thrombosis	0 - 24 hours post stent/scaffold implantation (note: time 0 is defined as the time point after the guiding catheter has been removed and the subject has left the catheterization lab)
Subacute device thrombosis	>24 hours - 30 days post stent/scaffold stent implantation
Early device thrombosis	0 - 30 days post stent/scaffold implantation (i.e. acute or subacute)
Late device thrombosis	30 days - 1 year post stent/scaffold implantation
Very late device thrombosis	>1-year post stent/scaffold implantation
Primary device thrombosis	A stent/scaffold thrombosis of a device which had not been re-treated since its original implant

Secondary device thrombosis	A stent/scaffold thrombosis after a stent/scaffold revascularization for restenosis or other non-thrombosis related events
Major adverse cardiovascular events	
The composite of cardiac death, all myocardial infarction, or ischemia-driven target lesion revascularization	
Patient-oriented composite endpoint	
The composite of all death, all myocardial infarction, or all revascularization	
Target lesion failure	
The composite of cardiac death, myocardial infarction attributable to the target vessel, or ischemia-driven target lesion revascularization	
Target vessel failure	
The composite of cardiac death, all myocardial infarction, or ischemia-driven target vessel revascularization	

*All sites were required to routinely measure CK-MB to assess peri-procedural MI. At least two post-procedure CK-MB draws were required, between 6 and 12 hours post-procedure and between 18 and 24 hours post-procedure. Troponins were not utilized for peri-procedural MI assessment.

1. Modified from 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;62:1563-70.
2. Baseline CK-MB value is required before study procedure and presumes a typical rise and fall post procedure to diagnose a peri procedure MI.
3. Whenever at least one baseline and one post procedure CK-MB measure are available in a patient with stable CAD, adjudication of MI will be based solely on these biomarker values. If the patient has stable ischemic heart disease and the baseline CK-MB measures are not available, they will be assumed to be within normal limits and MI will be adjudicated by the CEC solely according to the post procedure CK-MB measures.
4. From Cutlip DE, Windecker S, Mehran R, et al. Clinical end points in coronary stent trials: a case for standardized definitions. Circulation. 2007;115:2344-51.

CK-MB, creatine kinase, MB fraction; ECG, electrocardiography; ID, ischemia-driven; LBBB, left bundle branch block; MACE, major adverse cardiovascular events; MI, myocardial infarction; Non-TLR TVR, non-target lesion target vessel revascularization; Non-TVR, non-target vessel revascularization; POCE, patient oriented composite endpoint; TLF, target lesion failure; TLR, target lesion revascularization; TV, target vessel; TVF, target vessel failure; TVR, target vessel; ULN, upper limits of the local laboratory normal (collected from each hospital laboratory prior to study commencement).

Reprinted from Stone GW, Ellis SG, Gori T, et al. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. Lancet. 2018;392:1530-1540.

Table S4. Procedural outcomes in the randomized groups

	Absorb BVS	Xience CoCr-EES	P-value
During procedure			
Per patient	N=1296	N=1308	
- Bivalirudin use	344/1296 (26.5%)	362/1308 (27.7%)	0.52
- Glycoprotein IIb/IIIa inhibitor use	174/1296 (13.4%)	165/1308 (12.6%)	0.54
- Cangrelor use	4/1296 (0.3%)	6/1308 (0.5%)	0.75
Number of vessels treated*	1.1 ± 0.3	1.1 ± 0.3	0.64
- 1	1128/1292 (87.3%)	1135/1307 (86.8%)	0.72
- 2	164/1292 (12.7%)	170/1307 (13.0%)	0.81
- 3	0/1292 (0%)	2/1307 (0.2%)	0.50
Number of lesions treated*	1.2 ± 0.4	1.2 ± 0.5	0.66
- 1	1049/1292 (81.2%)	1061/1307 (81.2%)	0.99
- 2	226/1292 (17.5%)	220/1307 (16.8%)	0.66
- ≥3	17/1292 (1.3%)	26/1307 (2.0%)	0.18
Any assigned study device implanted	1236/1296 (95.4%)	1299/1308 (99.3%)	<0.0001
Only assigned study devices implanted	1200/1296 (92.6%)	1298/1308 (99.3%)	<0.0001
Any unassigned device implanted	90/1296 (6.9%)	7/1308 (0.5%)	<0.0001
Only unassigned devices implanted	54/1296 (4.2%)	6/1308 (0.5%)	<0.0001
Unplanned overlapping devices	76/1296 (5.9%)	60/1308 (4.6%)	0.14
Pre-dilatation performed	1291/1292 (99.9%)	1304/1307 (99.8%)	0.62
Post-dilatation performed	1088/1290 (84.3%)	714/1305 (54.7%)	<0.0001
Intravascular imaging guidance	201/1291 (15.6%)	167/1306 (12.8%)	0.04
Procedure duration (min)	46.2 ± 25.2	38.1 ± 21.1	<0.0001
Per lesion	L=1446	L=1457	
- Total study device length (mm)	20.5 ± 8.3	20.1 ± 7.9	0.25
- Maximum device† diameter (mm)	3.22 ± 0.44	3.16 ± 0.44	<0.0001
- Maximum device†/vessel diameter ratio	1.12 ± 0.12	1.10 ± 0.11	<0.0001
- Post-dilatation performed	1195/1446 (82.6%)	788/1457 (54.1%)	<0.0001
- Maximum device† pressure (atm.)	16.3 ± 3.1	15.9 ± 3.1	0.002
- Device success	1347/1424 (94.6%)	1436/1450 (99.0%)	<0.0001
Post-procedure			
Per patient	N=1,296	N=1,308	

- Procedure success	1203/1282 (93.8%)	1250/1303 (95.9%)	0.02
Per vessel (core laboratory)	V=1368	V=1382	
- TIMI flow			
- 0/1	1/1360 (0.1%)	0/1369 (0%)	0.50
- 2	25/1360 (1.8%)	28/1369 (2.0%)	0.70
- 3	1334/1360 (98.1%)	1341/1369 (98.0%)	0.80
Per lesion (core laboratory)	L=1446	L=1457	
- In-device measures			
- Acute gain (mm)	1.85 ± 0.46	1.92 ± 0.46	<0.0001
- Minimum luminal diameter (mm)	2.66 ± 0.39	2.74 ± 0.41	<0.0001
- Diameter stenosis (%)	9.9 ± 8.3	7.2 ± 7.9	<0.0001
- In-segment measures			
- Acute gain (mm)	1.59 ± 0.47	1.60 ± 0.46	0.72
- Minimum luminal diameter (mm)	2.41 ± 0.40	2.41 ± 0.41	0.71
- Diameter stenosis (%)	18.6 ± 8.5	18.2 ± 8.4	0.26

*Randomized target lesions (or vessels) plus non-randomized non-target lesions (or vessels). †Stent or scaffold or post-dilatation balloon. BVS = bioresorbable vascular scaffolds. CoCr-EES = everolimus-eluting stents. N = number of patients. V = number of vessels. L = number of target lesions. Reprinted from Stone GW, Ellis SG, Gori T, et al. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. Lancet. 2018;392:1530-1540.

Table S5. Results of the blinding and perception questionnaire at discharge and 1 year

Question	At discharge			At 1 year		
	Absorb BVS (N=1296)	Xience CoCr-EES (N=1308)	P-value	Absorb BVS (N=1296)	Xience CoCr-EES (N=1308)	P-value
Do you think you know which device you received?						
- Yes	133/1206 (11.0%)	114/1207 (9.4%)	0.20	183/993 (18.4%)	169/1031 (16.4%)	0.23
- No	1073/1206 (89.0%)	1093/1207 (90.6%)	0.20	810/993 (81.6%)	862/1031 (83.6%)	0.23
If yes, which device do you think you received?						
- Standard metal stent	14/127 (11.0%)	6/111 (5.5%)	0.12	21/180 (11.7%)	28/160 (17.5%)	0.13
- Temporary dissolving stent	113/127 (89.0%)	105/111 (94.6%)	0.12	159/180 (88.3%)	132/160 (82.5%)	0.13
If yes, are you certain?						
- Yes	32/126 (25.4%)	39/111 (35.1%)	0.10	92/178 (51.7%)	60/161 (37.3%)	0.008
- No	94/126 (74.6%)	72/111 (64.9%)	0.10	86/178 (48.3%)	101/161 (62.7%)	0.008
If yes, why do you think you know?						
- I was told by/overheard the doctor who did the procedure	16/130 (12.3%)	15/110 (13.6%)	0.76	28/179 (15.6%)	20/168 (11.9%)	0.31
- I was told by/overheard another person in the procedure room/cath lab	13/130 (10.0%)	10/110 (9.1%)	0.81	13/179 (7.3%)	9/168 (5.4%)	0.47
- I was told by/overheard another person in the hospital before discharge	6/130 (4.6%)	7/110 (6.4%)	0.55	7/179 (3.9%)	11/168 (6.5%)	0.27
- I was told by/overheard a family member or friend who was told	5/130 (3.8%)	0/110 (0%)	0.04	6/179 (3.4%)	0/168 (0%)	0.02
- I believe so because I am feeling better	24/130 (18.5%)	16/110 (14.5%)	0.42	18/179 (10.1%)	17/168 (10.1%)	0.98
- I believe so because I am not feeling better	0/130 (0%)	0/110 (0%)	-	1/179 (0.6%)	3/168 (1.8%)	0.28
- Other*	66/130 (50.8%)	62/110 (56.4%)	0.39	106/179 (59.2%)	108/168 (64.3%)	0.33

*Most common reason given was guess/hope/intuition. Reprinted from Stone GW, Ellis SG, Gori T, et al. Blinded outcomes and angina assessment of coronary bioresorbable scaffolds: 30-day and 1-year results from the ABSORB IV randomised trial. Lancet. 2018;392:1530-1540.

Table S6. Medication use through 5-year follow-up

	Absorb BVS (n=1296)	Xience CoCr-EES (n=1308)	Difference (95% CI)	P value
Aspirin				
Total days taking, mean ± SD	1615 ± 465	1627 ± 454	-12 [-48, 23]	0.50
Use on day 30 (1 month)*	1285/1287 (99.8%)	1295/1301 (99.5%)		0.29
Use on day 365 (1 year)*	1216/1238 (98.2%)	1236/1259 (98.2%)		0.93
Use on day 730 (2 years)*	1174/1209 (97.1%)	1191/1232 (96.7%)		0.54
Use on day 1095 (3 years)*	1121/1174 (95.5%)	1147/1204 (95.3%)		0.80
Use on day 1460 (4 years)*	1075/1140 (94.3%)	1105/1163 (95.0%)		0.45
Use on day 1825 (5 years)*	1024/1099 (93.2%)	1064/1118 (95.2%)		0.045
P2Y12 inhibitor				
Total days taking, mean ± SD	1101 ± 655	1110 ± 656	-9 [-60, 41]	0.72
Use on day 30 (1 month)*	1280/1287 (99.5%)	1295/1301 (99.5%)		0.77
Use on day 365 (1 year)*	1147/1238 (92.6%)	1185/1259 (94.1%)		0.14
Use on day 730 (2 years)*	740/1209 (61.2%)	752/1232 (61.0%)		0.93
Use on day 1095 (3 years)*	646/1174 (55.0%)	653/1204 (54.2%)		0.70
Use on day 1460 (4 years)*	582/1140 (51.1%)	598/1163 (51.4%)		0.86
Use on day 1825 (5 years)*	538/1099 (49.0%)	555/1118 (49.6%)		0.75
Dual anti-platelet therapy				
Total days taking, mean ± SD	1070 ± 652	1076 ± 655	-6 [-57, 44]	0.81
Use on day 30 (1 month)*	1279/1287 (99.4%)	1289/1301 (99.1%)		0.38
Use on day 365 (1 year)*	1133/1238 (91.5%)	1170/1259 (92.9%)		0.19
Use on day 730 (2 years)*	720/1209 (59.6%)	732/1232 (59.4%)		0.94
Use on day 1095 (3 years)*	616/1174 (52.5%)	620/1204 (51.5%)		0.63
Use on day 1460 (4 years)*	551/1140 (48.3%)	562/1163 (48.3%)		1.00
Use on day 1825 (5 years)*	504/1099 (45.9%)	520/1118 (46.5%)		0.76
Chronic oral anticoagulation				
Use on day 30 (1 month)*	13/1287 (1.0%)	8/1301 (0.6%)		0.26
Use on day 365 (1 year)*	22/1238 (1.8%)	17/1259 (1.4%)		0.39

Use on day 730 (2 years)*	32/1209 (2.6%)	28/1232 (2.3%)	0.55
Use on day 1095 (3 years)*	46/1174 (3.9%)	38/1204 (3.2%)	0.31
Use on day 1460 (4 years)*	56/1140 (4.9%)	44/1163 (3.8%)	0.18
Use on day 1825 (5 years)*	63/1099 (5.7%)	48/1118 (4.3%)	0.12
Angiotensin converting enzyme inhibitors, angiotensin receptor blockers or renin inhibitors			
Use on day 30 (1 month)*	835/1287 (64.9%)	833/1301 (64.0%)	0.65
Use on day 365 (1 year)*	791/1238 (63.9%)	791/1259 (62.8%)	0.58
Use on day 730 (2 years)*	757/1209 (62.6%)	773/1232 (62.7%)	0.95
Use on day 1095 (3 years)*	720/1174 (61.3%)	745/1204 (61.9%)	0.78
Use on day 1460 (4 years)*	699/1140 (61.3%)	723/1163 (62.2%)	0.67
Use on day 1825 (5 years)*	673/1099 (61.2%)	696/1118 (62.3%)	0.62
Beta-blocker			
Use on day 30 (1 month)*	915/1287 (71.1%)	924/1301 (71.0%)	0.97
Use on day 365 (1 year)*	827/1238 (66.8%)	860/1259 (68.3%)	0.42
Use on day 730 (2 years)*	800/1209 (66.2%)	812/1232 (65.9%)	0.89
Use on day 1095 (3 years)*	764/1174 (65.1%)	777/1204 (64.5%)	0.78
Use on day 1460 (4 years)*	735/1140 (64.5%)	757/1163 (65.1%)	0.76
Use on day 1825 (5 years)*	702/1099 (63.9%)	739/1118 (66.1%)	0.27
Calcium channel blocker			
Use on day 30 (1 month)*	261/1287 (20.3%)	276/1301 (21.2%)	0.56
Use on day 365 (1 year)*	275/1238 (22.2%)	267/1259 (21.2%)	0.54
Use on day 730 (2 years)*	270/1209 (22.3%)	279/1232 (22.6%)	0.85
Use on day 1095 (3 years)*	268/1174 (22.8%)	279/1204 (23.2%)	0.84
Use on day 1460 (4 years)*	261/1140 (22.9%)	275/1163 (23.6%)	0.67
Use on day 1825 (5 years)*	252/1099 (22.9%)	276/1118 (24.7%)	0.33
Nitrates			
Use on day 30 (1 month)*	407/1287 (31.6%)	399/1301 (30.7%)	0.60
Use on day 365 (1 year)*	394/1238 (31.8%)	403/1259 (32.0%)	0.92
Use on day 730 (2 years)*	388/1209 (32.1%)	397/1232 (32.2%)	0.94
Use on day 1095 (3 years)*	389/1174 (33.1%)	389/1204 (32.3%)	0.67

Use on day 1460 (4 years)*	392/1140 (34.4%)	375/1163 (32.2%)	0.28
Use on day 1825 (5 years)*	370/1099 (33.7%)	364/1118 (32.6%)	0.58
Ranolazine			
Use on day 30 (1 month)*	11/1287 (0.9%)	19/1301 (1.5%)	0.15
Use on day 365 (1 year)*	19/1238 (1.5%)	26/1259 (2.1%)	0.32
Use on day 730 (2 years)*	22/1209 (1.8%)	29/1232 (2.4%)	0.36
Use on day 1095 (3 years)*	19/1174 (1.6%)	27/1204 (2.2%)	0.27
Use on day 1460 (4 years)*	18/1140 (1.6%)	30/1163 (2.6%)	0.09
Use on day 1825 (5 years)*	16/1099 (1.5%)	27/1118 (2.4%)	0.10
Statin			
Use on day 30 (1 month)*	1125/1287 (87.4%)	1163/1301 (89.4%)	0.12
Use on day 365 (1 year)*	1060/1238 (85.6%)	1099/1259 (87.3%)	0.22
Use on day 730 (2 years)*	1027/1209 (84.9%)	1068/1232 (86.7%)	0.22
Use on day 1095 (3 years)*	996/1174 (84.8%)	1040/1204 (86.4%)	0.28
Use on day 1460 (4 years)*	965/1140 (84.6%)	1002/1163 (86.2%)	0.31
Use on day 1825 (5 years)*	928/1099 (84.4%)	961/1118 (86.0%)	0.31
Other lipid-lowering agent			
Use on day 30 (1 month)*	136/1287 (10.6%)	129/1301 (9.9%)	0.58
Use on day 365 (1 year)*	133/1238 (10.7%)	147/1259 (11.7%)	0.46
Use on day 730 (2 years)*	138/1209 (11.4%)	150/1232 (12.2%)	0.56
Use on day 1095 (3 years)*	137/1174 (11.7%)	154/1204 (12.8%)	0.40
Use on day 1460 (4 years)*	139/1140 (12.2%)	160/1163 (13.8%)	0.26
Use on day 1825 (5 years)*	141/1099 (12.8%)	165/1118 (14.8%)	0.19

*±7 day window. BVS = bioresorbable vascular scaffolds. CoCr-EES = everolimus-eluting stents.

Figure S1. Patient screening, randomization and follow-up
BVS = bioresorbable vascular scaffolds. CoCr-EES = cobalt chromium everolimus-eluting stents. ITT = intention-to-treat.

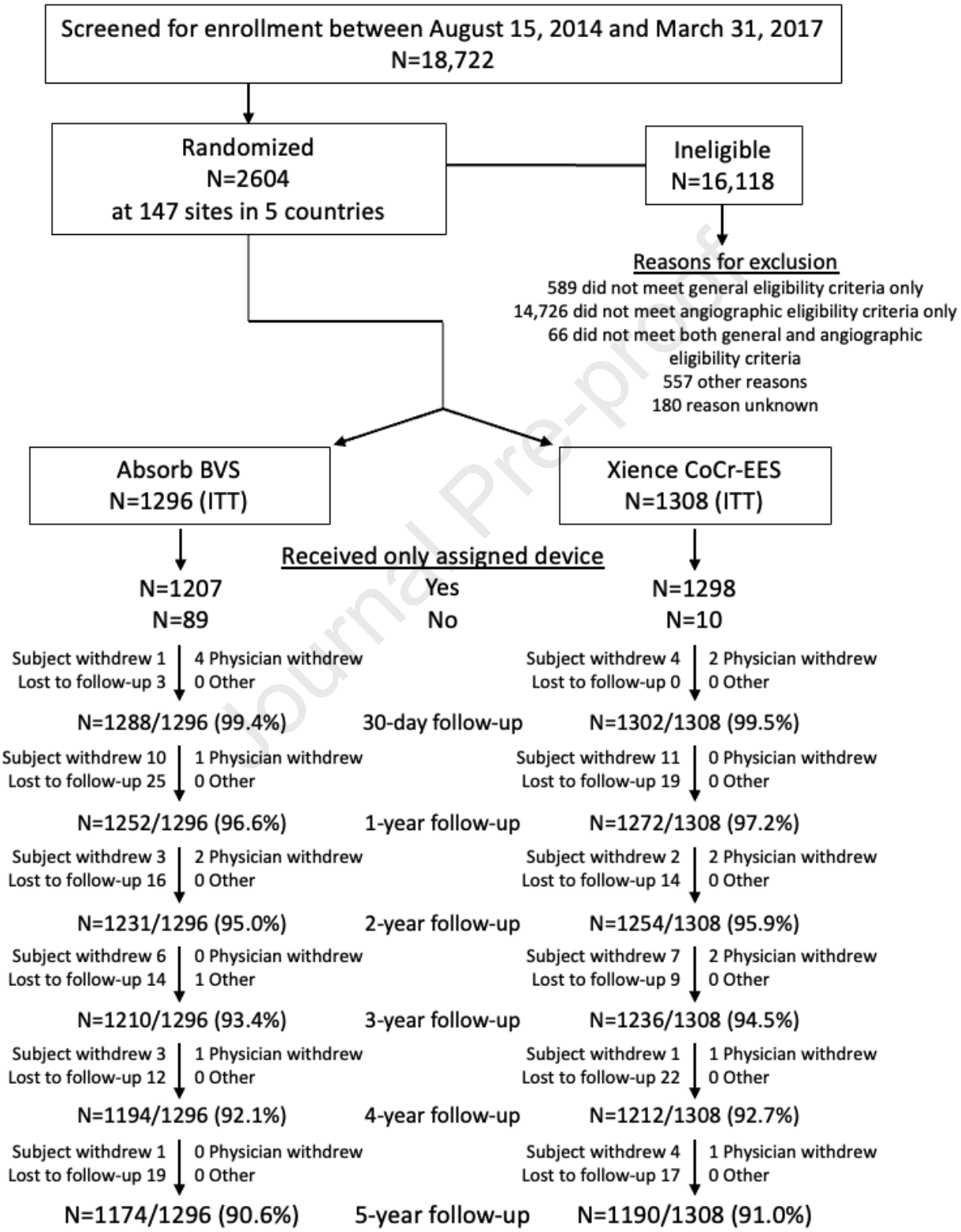


Figure S2. Subgroup analyses for the 5-year rate of target lesion failure.
Event rates under the BVS and CoCr-EES columns in parentheses are Kaplan-Meier estimates (%), so differ from the number of events within 5 years (numerator) divided by the number of patients at risk at time 0 (denominator). The P-value for interaction (P [Int]) represents the likelihood of interaction between the variable and the relative treatment effect. Patients with multiple target lesions were categorized into the vessel with either the smallest RVD or the longest lesion. BVS = bioresorbable vascular scaffolds. CoCr-EES = cobalt chromium everolimus-eluting stents. ACS = acute coronary syndrome. CAD = coronary artery disease. RVD = reference vessel diameter

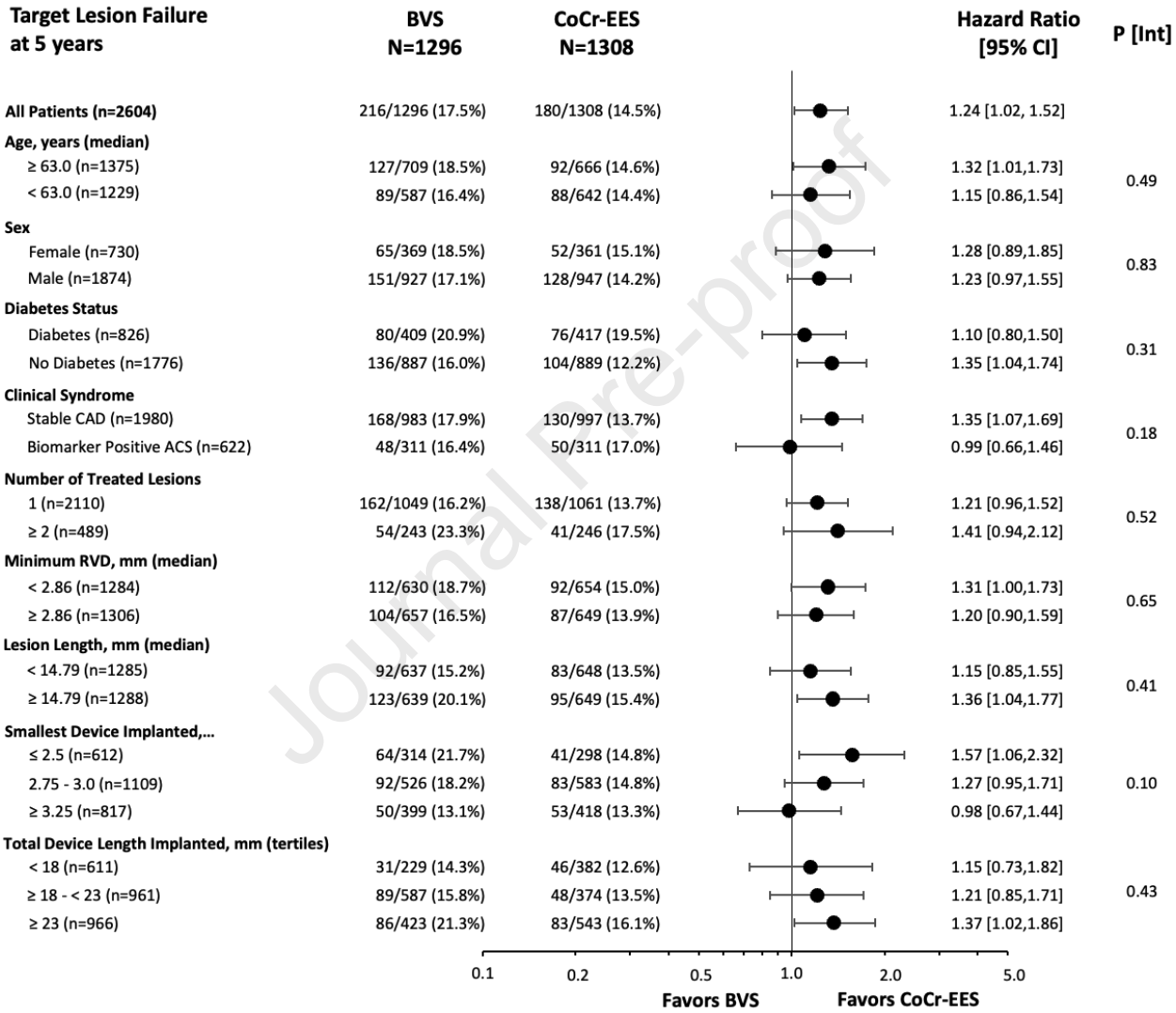


Figure S3. Results from the serial Seattle Angina Questionnaire and the EuroQOL-5D Visual Analog Scale assessments. The SAQ-7 Summary Score is the average of the Angina Frequency, Physical Limitation and Quality of Life subscales. There were no significant between-group differences between any of the values at any time point except in the EQ-5D VAS at 1 year (p=0.025) and at 2 years (p=0.03), favoring BVS. SAQ = Seattle Angina Questionnaire. EQ-5D VAS = EuroQOL-5D Visual Analog Scale.

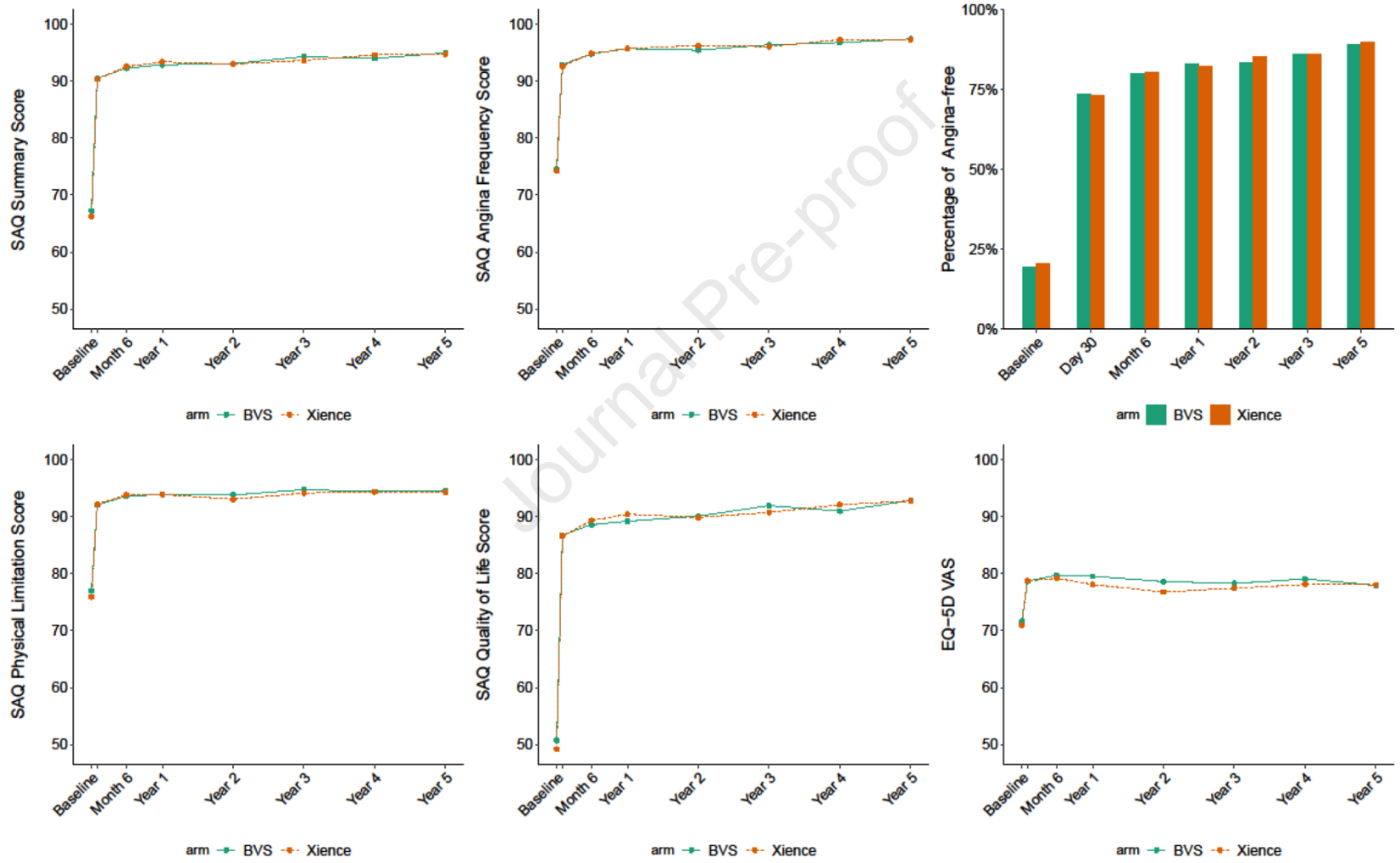
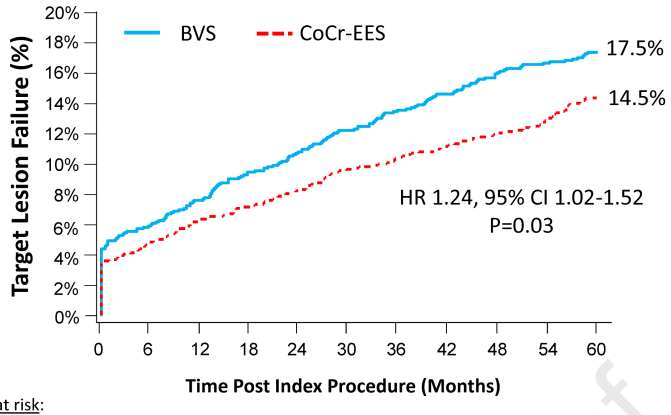


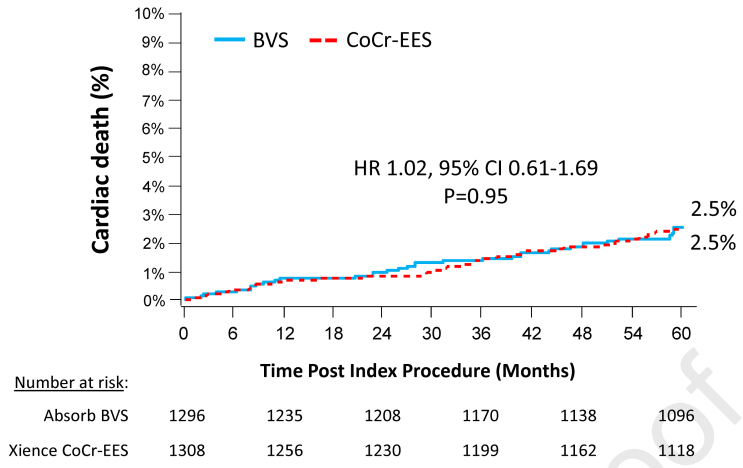
Figure 1A



Number at risk:

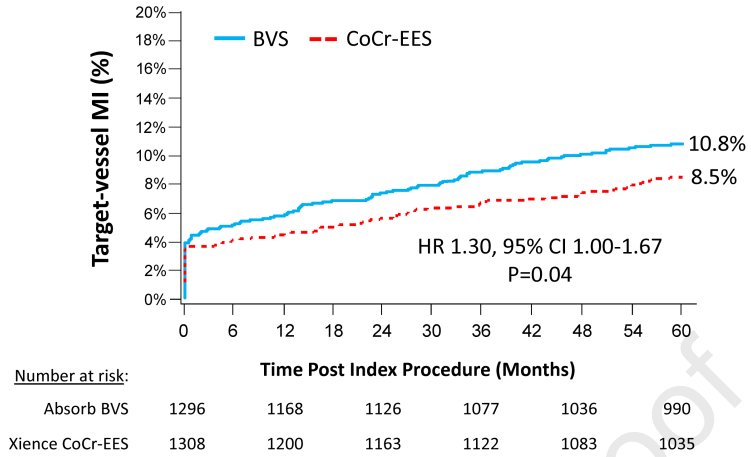
Absorb BVS	1296	1149	1086	1028	979	933
Xience CoCr-EES	1308	1183	1138	1088	1042	984

Figure 1B



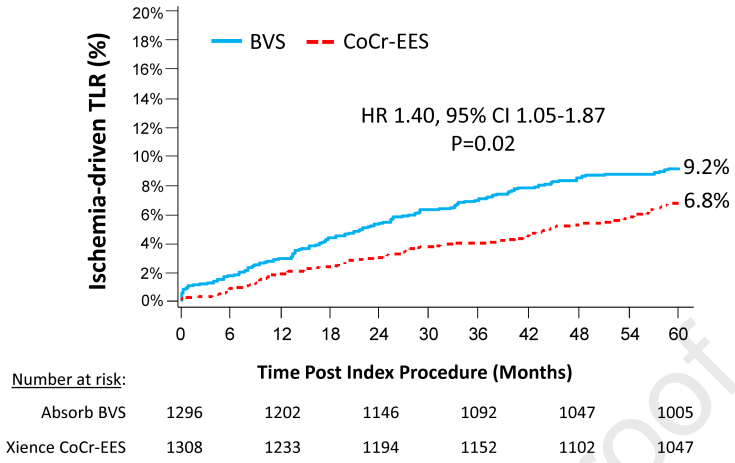
Number at risk:						
Absorb BVS	1296	1235	1208	1170	1138	1096
Xience CoCr-EES	1308	1256	1230	1199	1162	1118

Figure 1C



Number at risk:						
Absorb BVS	1296	1168	1126	1077	1036	990
Xience CoCr-EES	1308	1200	1163	1122	1083	1035

Figure 1D



Number at risk:						
Absorb BVS	1296	1202	1146	1092	1047	1005
Xience CoCr-EES	1308	1233	1194	1152	1102	1047

Figure 1E

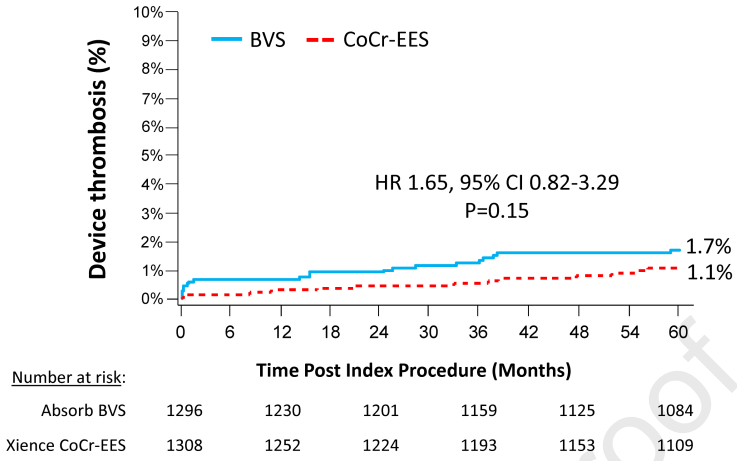
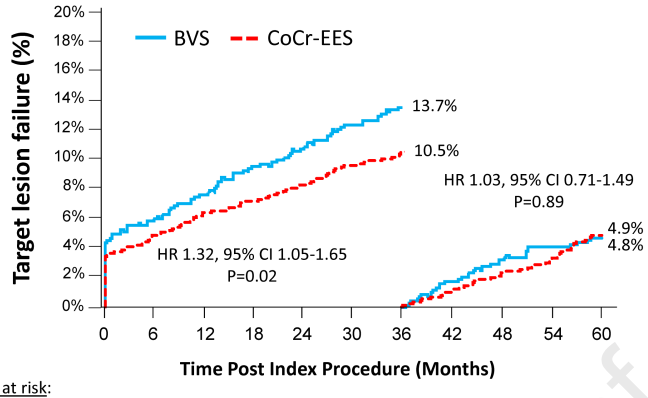


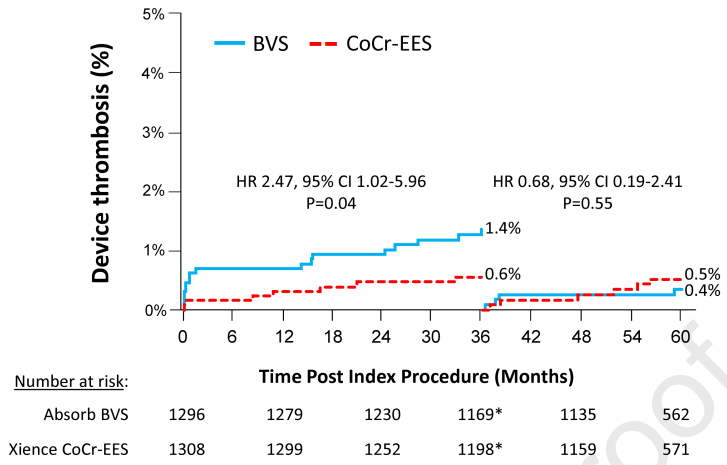
Figure 2A



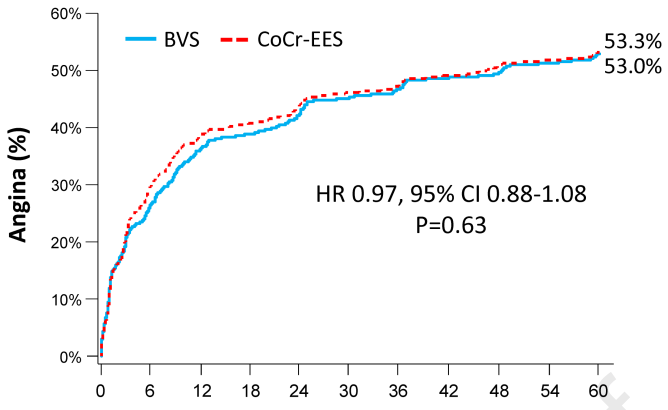
Number at risk:

Absorb BVS	1296	1149	1086	1169*	1109	547
Xience CoCr-EES	1308	1183	1138	1198*	1141	544

Figure 2B



Number at risk:						
Absorb BVS	1296	1279	1230	1169*	1135	562
Xience CoCr-EES	1308	1299	1252	1198*	1159	571



Number at risk:						
Absorb BVS	1296	787	693	621	573	519
Xience CoCr-EES	1308	768	688	630	572	528

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Five-Year Clinical Outcomes After Coronary Bioresorbable Scaffolds and Drug-Eluting Stents: The ABSORB IV Randomized Trial

Brief title: Late Outcomes of Bioresorbable Scaffolds

Gregg W. Stone, MD, Dean J. Kereiakes, MD, Tommaso Gori, MD, D. Christopher Metzger, MD, Bernardo Stein, MD, Matthew Erickson, MD, Jan Torzewski, MD, Ameer Kabour, MD, Guy Piegari, MD, Jeffrey Cavendish, MD, Barry Bertolet, MD, Kelly A. Stockelman PhD, Nick E.J. West MD, Ori Ben-Yehuda, MD, James W. Choi, MD, Steven O. Marx, MD, John A. Spertus, MD, MPH, and Stephen G. Ellis, MD, for the ABSORB IV Investigators*

From the Zena and Michael A. Wiener Cardiovascular Institute, Icahn School of Medicine at Mount Sinai, New York, NY (GWS); The Carl and Edyth Lindner Research Center at The Christ Hospital, Cincinnati, OH (DJK); Kardiologie I University Medical Center and DZHK Rhein-Main, Mainz, Germany (TG); Ballad Health Systems CVA Heart Institute, Kingsport, TN (DCM); Morton Plant Hospital, Clearwater, FL (BS); Fiona Stanley Hospital, Perth, Australia (ME); Cardiovascular Center Oberallgäu-Kempten, Kempten, Germany (JT); Mercy St. Vincent Medical Center, Toledo, OH (AK); Penn State Health Medical Group-Berks Cardiologists, Wyomissing, PA (GP); Scripps Memorial Hospital La Jolla, La Jolla, CA (JC); North Mississippi Medical Center, Tupelo, MS (BB); Abbott Vascular, Santa Clara, CA (KAS,

NEJW); University of California, San Diego, San Diego, CA (OBY); Texas Health Presbyterian Hospital and the Baylor Research Institute, Dallas, TX (JWC); NewYork-Presbyterian Hospital/Columbia University Medical Center, New York, NY (SOM); University of Missouri - Kansas City (UMKC) and Saint Luke's Mid America Heart Institute/University of Missouri - Kansas City (UMKC), Kansas City, MO (JAS); Cleveland Clinic, Cleveland, OH (SGE).

*The investigators, institutions and research organizations participating in A Clinical Evaluation of Absorb™ BVS, the Everolimus Eluting Bioresorbable Vascular Scaffold in the Treatment of Subjects with de novo Native Coronary Artery Lesions (ABSORB IV) trial are listed in reference 12.

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Address for correspondence:

Gregg W. Stone MD

Mount Sinai Medical Center

1 Gustave L. Levy Place

New York, NY 10029

Telephone: 212-241-6500

e-mail: gregg.stone@mountsinai.org

Twitter: @GreggWStone

Abstract

Background. Bioresorbable vascular scaffolds (BVS) were designed to improve late event-free survival compared with metallic drug-eluting stents. However, initial trials demonstrated worse early outcomes with BVS, in part due to suboptimal technique. In the large-scale, blinded ABSORB IV trial, polymeric everolimus-eluting BVS implanted with improved technique demonstrated non-inferior 1-year outcomes compared with cobalt chromium everolimus-eluting stents (CoCr-EES).

Objectives. To evaluate the long-term outcomes from the ABSORB IV trial.

Methods. We randomized 2,604 patients at 147 sites with stable or acute coronary syndromes to BVS with improved technique vs. CoCr-EES. Patients, clinical assessors and event adjudicators were blinded to randomization. Five-year follow-up was completed.

Results. Target lesion failure (TLF) at 5 years occurred in 216 patients (17.5%) assigned to BVS and 180 patients (14.5%) assigned to CoCr-EES (P=0.03). Device thrombosis within 5 years occurred in 21 (1.7%) BVS and 13 (1.1%) CoCr-EES patients (P=0.15). Event rates were slightly greater with BVS than CoCr-EES through 3-year follow-up and similar between 3-5 years. Angina, also centrally adjudicated, recurred within 5 years in 659 patients (cumulative rate 53.0%) assigned to BVS and 674 patients (53.3%) assigned to CoCr-EES (P=0.63).

Conclusions. In this large-scale, blinded randomized trial, despite improved implantation technique the absolute 5-year rate of TLF was 3% greater after BVS compared with CoCr-EES. The risk period for increased events was restricted to 3 years, the time point of complete scaffold bioresorption; event rates were similar thereafter. Angina recurrence after intervention was frequent during 5-year follow-up but was comparable with both devices.

Condensed abstract: To determine whether the long-term outcomes of first-generation polymeric bioresorbable vascular scaffolds (BVS) implanted with improved technique are similar to contemporary metallic drug-eluting stents, we performed a blinded randomized trial in which 2,604 patients were assigned to BVS with improved technique vs. cobalt chromium everolimus-eluting stents (CoCr-EES). At 5-year follow-up, rates of target lesion failure (TLF) were higher with BVS than CoCr-EES (17.5% vs. 14.5%, P=0.03). TLF and device thrombosis rates were greater with BVS than CoCr-EES through 3-year follow-up and similar between 3-5 years. Angina recurred frequently within 5 years but was similar with both devices.

Key words: Stent, bioresorbable scaffold, randomized trial, coronary artery disease, prognosis, angina

Abbreviations

ACS = acute coronary syndromes

BVS = bioresorbable vascular scaffolds

CoCr-EES = cobalt chromium everolimus-eluting stents.

DES = drug-eluting stents

ID-TLR = ischemia-driven target lesion revascularization

MACE = major adverse cardiac events

MI = myocardial infarction.

PoCE = patient-oriented composite endpoint

TLF = target lesion failure

TVF = target vessel failure

Clinical Trial: ClinicalTrials.gov number NCT02173379

Introduction

Metallic drug-eluting stents (DES) prevent recoil and inhibit restenosis within the first year after coronary artery implantation, thereby improving outcomes in patients with coronary artery disease. However, metallic DES permanently cage the coronary artery, impair cyclic pulsatility and vasomotion, and serve as a rigid frame within which neointimal proliferation and neoatherosclerosis may develop, chronically narrowing the stent lumen. Longitudinal studies have demonstrated an ongoing ~2% per year rate of very late (>1-year) metallic stent-related adverse events (restenosis and less commonly stent thrombosis) that continues for at least 15 years.[1,2] Drug-eluting bioresorbable vascular scaffolds (BVS) were designed to provide the early mechanical support functions of a metallic DES and then completely resorb over the next several years, normalizing vascular structure and function and removing the nidus for very late adverse events.[3,4] BVS have also been shown to "un-jail" covered side branches, "un-jacket" long treated segments (restoring late surgical options), "un-layer" treated in-stent restenosis, eliminate artifacts with non-invasive imaging (e.g. computed tomographic angiography), and address individual patients' cultural, religious, or personal preferences to avoid a permanent implant.[3] One early randomized trial even reported lower rates of recurrent angina with BVS compared with DES, although the lack of blinding led to uncertainty regarding this post hoc finding.[5]

The most widely studied bioresorbable scaffold is the Absorb everolimus-eluting poly(L-lactide) BVS. Unfortunately, most randomized trials demonstrated an increase in early adverse event rates with this device compared with metallic DES.[3,4,6-8] This risk was limited to the first 3 years after BVS implantation, coinciding with the time of its complete bioresorption; thereafter, event rates were similar with BVS and DES.[9] The higher 3-year event rates with BVS have been attributed to suboptimal mechanical properties of the first-generation scaffold (thick struts (~157

μm), limited expansion range with propensity to fracture, and greater recoil). Suboptimal implantation technique has also contributed to increased adverse event rates with BVS. Specifically, BVS outcomes were improved if vessels were appropriately sized (avoiding very small (<2.25 mm) or very large (>4.0 mm) reference vessel diameters [RVD]), if lesion pre-dilatation and preparation were adequate, and if post-dilatation was routinely performed at high-pressure with non-compliant balloons.[10,11]

To address these issues, we performed the ABSORB IV trial, the largest (n=2,604) randomized trial of any BVS vs. metallic DES to date.[12] Novel aspects of this trial included: 1) active investigator training and monitoring during patient recruitment to ensure patients with very small (or large) target vessels were not enrolled; 2) mandatory target lesion pre-dilatation and strong recommendation for high-pressure non-compliant balloon post-dilatation; 3) inclusion of patients with acute coronary syndromes (ACS) who typically have soft, lipid-rich lesions that might respond well to BVS;[13-15] 4) frequent assessment and adjudication of all possible angina and anginal equivalent symptoms; and 5) blinding of all patients, their families, research and healthcare personnel and outcomes assessors after the procedure completion to minimize bias. Early results from this trial demonstrated that the Absorb poly(L-lactide) everolimus-eluting BVS was non-inferior to the Xience cobalt chromium everolimus-eluting stent (CoCr-EES) at 30 days and 1 year for target lesion failure (TLF) and angina.[12] Longer-term outcomes from this trial have not been described. We herein report the final 5-year outcomes from the ABSORB IV randomized trial.

Methods

Study design. ABSORB IV was a multicenter, blinded, active-treatment-controlled randomized trial that enrolled patients from 5 countries (U.S., Canada, Germany, Australia, and

Singapore). The study organization and participating centers have been previously reported[12] and are listed in the Appendix. The protocol was designed by the principal investigators and sponsor (Abbott Vascular, Santa Clara, CA), in concert with the U.S. Food and Drug Administration (FDA). The study protocol was approved by the institutional review board or ethics committee at each participating center. The sponsor funded the trial, was involved in protocol design, site selection and management, and data analysis. The principal investigators had unrestricted data access, prepared the manuscript and vouch for the accuracy and completeness of the reported data. The ABSORB IV trial is registered at ClinicalTrials.gov Identifier: NCT01751906.

Patients, procedures, blinding and follow-up. Complete inclusion and exclusion criteria are shown in Appendix Table S1. Patients ≥18 years of age with stable ischemic heart disease or ACS (unstable angina, non-ST-segment elevation MI or recent ST-segment elevation MI undergoing percutaneous coronary intervention (PCI) of one, two or three *de novo* native coronary artery lesions in up to two epicardial coronary arteries were enrolled. Each lesion was ≤24 mm in length and had RVD 2.5-3.75 mm by visual assessment. Eligible patients were randomized to receive the Absorb BVS or Xience CoCr-EES (both Abbott Vascular). The PCI procedure has been previously described.[12] BVS pre-dilatation was mandatory, and high-pressure post-dilatation with a non-compliant balloon sized up to 0.5 mm larger than the nominal scaffold diameter was strongly encouraged. Dual antiplatelet therapy (DAPT) was continued for at least one year, and aspirin indefinitely.

Patients were blinded to randomization arm by use of conscious sedation and music-playing headphones. Clinical follow-up was performed by blinded personnel not present at the index procedure. The success of blinding was assessed at discharge and 1 year by administration of a patient blinding questionnaire.[12] Clinical follow-up was performed at 30 days, 1 year and

then annually through 5 years. In addition to standard clinical assessments, at each follow-up visit patients were asked detailed questions about the presence, frequency, characteristics, severity and inciting features of all possible angina or anginal equivalent symptoms at any time since the last visit using a custom 6-page script, as previously described.[12] Quality-of-life (QoL) was also assessed at baseline, 6 months and then at each annual visit with the Seattle Angina Questionnaire (SAQ)-7 and the EuroQOL-5D Visual Analog Scale (EQ-5D VAS).

Outcomes. Cardiac events and angina classification and severity were adjudicated by an independent clinical events committee (CEC) blinded to treatment assignment. The primary endpoint was TLF, a composite of cardiac death, target-vessel myocardial infraction (MI) or ischemia-driven target lesion revascularization (ID-TLR) at 30 days. Major secondary endpoints were TLF and adjudicated angina at 1 year, the latter consisting of typical angina or anginal equivalent symptoms. Other composite measures assessed included target vessel failure (TVF), major adverse cardiac events (MACE), and the patient-oriented composite endpoint (PoCE). The components of these and other pre-specified secondary endpoints and detailed endpoint definitions are listed in Appendix Tables S2 and S3.

Statistical analysis. An intended sample size of 2600 patients was sufficient to determine whether BVS was non-inferior to CoCr-EES for the primary endpoint of 30-day TLF, as previously described.[12] Secondary endpoints through 5-year follow-up, the subject of the present report, were not specifically powered. Categorical variables were compared by Chi-squared test or Fisher's exact test. Continuous variables were compared by t-test. All principal analyses were performed in the intention-to-treat population, consisting of all patients randomized, regardless of treatment received. Time-to-first event rates were estimated using Kaplan-Meier methodology and compared by log-rank test. Hazard ratios (HR) and 95% confidence intervals (CI) were

calculated from a univariable Cox model. Consistency of device treatment effects for TLF at 5 years was examined with formal interaction testing in relevant subgroups. Landmark analysis was performed at 3 years to determine whether relative device effects varied before and after 3 years, the timepoint of complete BVS bioresorption, as previously described.[9] A two-sided P-value <0.05 was considered significant for all superiority testing. All statistical analyses were performed using SAS v9.4 (SAS Institute, Cary, NC).

Results

Patients and procedures. Between August 15, 2014, and March 31, 2017, 2604 patients were randomized at 147 sites to Absorb BVS (n=1296) or Xience CoCr-EES (n=1308) (Appendix Figure S1). The baseline clinical and angiographic characteristics of the groups were well matched (Table 1). Procedural outcomes are shown in Appendix Table S4. Only 78/2893 (2.7%) treated lesions had a RVD <2.25 mm by quantitative coronary analysis. Pre-dilatation and post-dilatation were performed in 1291/1292 (99.9%) and 1088/1290 (84.3%) of BVS-treated lesions respectively. Maximum device to vessel diameter ratios were greater with BVS than CoCr-EES, as was maximum device pressure. Nonetheless, mean in-device acute gain was lower and residual diameter stenosis was higher with BVS compared with CoCr-EES, and device and procedural success rates were correspondingly lower in the BVS group. Intravascular imaging guidance was used in only 201/1291 (15.6%) BVS and 167/1306 (12.8%) CoCr-EES procedures (P=0.04).

Clinical outcomes. As previously reported,[12] most patients were effectively blinded to their treatment assignment at discharge and 1 year (Appendix Table S5). Five-year follow-up was complete in 1174 (90.6%) BVS patients and in 1190 (91.0%) CoCr-EES patients (Appendix

Figure S1). Use of anti-platelet, anti-anginal and lipid-lowering agents were similar with both devices during follow-up (Appendix Table S6).

Five-year outcomes are shown in Table 2 and Figure 1. TLF at 5 years occurred in 216 patients (Kaplan-Meier rate 17.5%) assigned to BVS and 180 patients (14.5%) assigned to CoCr-EES (HR 1.24, 95% CI 1.02-1.52, P=0.03). This difference was driven by increased rates of target-vessel MI and ID-TLR after BVS, whereas the 5-year rates of cardiac and all-cause death after BVS and CoCr-EES were similar. There were no significant differences in the rates of TVF, MACE or the PoCE among patients treated with BVS compared with CoCr-EES. Nor were there significant differences in the rates of device thrombosis within 5 years after BVS and CoCr-EES (21 events (1.7%) vs. 13 (1.1%) events respectively, HR 1.65, 95% CI 0.82-3.29; P=0.15).

In landmark analysis, TLF and device thrombosis rates were higher with BVS compared with CoCr-EES within the first 3 years after treatment, and similar between 3 and 5 years (Figure 2). The relative hazards of BVS vs CoCr-EES for the 5-year rate of TLF were consistent across all pre-specified subgroups (Appendix Figure S2).

Angina recurrence and quality-of-life. By 5 years, adjudicated angina or angina equivalent symptoms had recurred in 659 patients treated with BVS (53.0%) and in 674 patients (53.3%) treated with CoCr-EES (HR 0.97, 95% CI 0.88-1.08; P=0.63) (Figure 3 and Table 3). The rates of angina at each annual follow-up visit were substantially less but again did not differ between the two devices (Table 4). Nor were there differences in the SAQ overall summary or component scores or the EuroQOL-5D between BVS and CoCr-EES (Appendix Figure S3).

Discussion

In the blinded randomized ABSORB IV trial, the largest randomized trial of BVS to date, polymeric everolimus-eluting Absorb BVS implanted in an expanded patient population and with improved lesion selection and technique (compared with most prior studies) were non-inferior to Xience CoCr-EES for the rates of TLF at 30 days and TLF and recurrent angina at 1 year.[12] With follow-up now complete through 5 years, the principal long-term outcomes from this trial (as summarized in the Central Illustration) are as follows: 1) Patients treated with BVS had higher 5-year rates of TLF compared with CoCr-EES (3.0% absolute difference), driven by increased rates of TV-MI and ID-TLR, although the risk period for TLF was confined to the first 3 years; 2) In contrast, the 5-year rates of other composite outcomes, including TVF, MACE and the PoCE, were not significantly higher with BVS compared with CoCr-EES; 3) Overall 5-year device thrombosis rates were also not significantly different with BVS compared with CoCr-EES, although device thrombosis rates were 0.8% higher within 3 years after treatment and then similar thereafter; 4) Adjudicated typical angina or anginal equivalent symptoms recurred in >50% of patients within 5 years after PCI in this trial, although with nearly identical frequency between BVS and CoCr-EES; and 5) Conversely, the rates of typical angina or anginal equivalent symptoms measured at any discrete time point were much lower (<10%), but again were similar after BVS and CoCr-EES; 6) QoL measures during 5-year follow-up as assessed by the SAQ and the EuroQOL-5D were also similar between devices.

In the present study BVS were evaluated in an expanded patient population enriched with ACS (~50% of patients) and compared with the prior ABSORB trials were implanted with improved lesion selection and techniques based on insights from earlier studies.[10] While the 5-year rates of TLF remained higher with BVS than CoCr-EES, the absolute difference was only 3.0%, a relatively modest increase given the 5-year timeframe. In addition, other commonly used

composite endpoints that reflect overall patient outcomes, including MACE, TVF and PoCE, were not significantly different between the devices, occurring in only ~2% more patients within 5 years treated with BVS. Improved patient and lesion selection (especially the near elimination of lesions with RVD <2.25 mm, the leading cause of adverse outcomes with the Absorb BVS in prior trials),[10] and optimized technique (including routine lesion preparation and high-pressure post-dilatation in ~85% of lesions) were likely responsible for these improved results.

Similar to that reported from four prior ABSORB randomized trials, the risk period for BVS in ABSORB IV ended at 3 years, the approximate time of complete bioresorption of the scaffold.[9] Within this initial 3-year period TLF and device thrombosis occurred in 3.2% and 0.8% more patients treated with BVS than CoCr-EES. BVS outcomes in this 3-year risk period may be further improved by the routine use of intravascular imaging, which was used to guide scaffold implantation in only 15.6% of BVS patients. Intravascular imaging may improve outcomes even more so with BVS than with metallic DES by ensuring both 1) maximal device expansion, and 2) acute scaffold apposition to the vessel wall, thereby promoting endothelial coverage of the resorbable struts which may prevent intraluminal scaffold dismantling during bulk erosion, the leading cause of the excess risk of thrombosis with BVS.[16,17] DAPT use at 3 years was 48% in both groups. While the administration of DAPT for 3 years in all BVS patients may be considered, prolonged DAPT beyond 1 year has not been associated with decreased scaffold thrombosis.[18]

Despite improved lesion selection and implantation technique in the present study, the in-device acute gain was less and the residual diameter stenosis was greater after BVS compared with CoCr-EES, likely contributing to the increased risk of events prior to complete scaffold bioresorption. Outcomes would likely be improved with scaffolds with better expansion

characteristics and lower recoil than the first generation BVS, and with thinner struts to improve fluid dynamics and promote more rapid and complete endothelization. For example, the Firesorb sirolimus-eluting polymeric BVS has 100-125 μm strut thickness. In the FUTURE-II randomized trial (n=433), this device had nearly identical angiographic in-segment late loss and tissue strut coverage by optical coherence tomography as CoCr-EES at 1 year, with 0.9% and 1.9% TLF rates, respectively, and no scaffold thrombosis.[19] A 99-μm strut thickness poly(L-lactide) everolimus-eluting BVS with improved mechanical properties has been developed (Esprit-BTK, Abbott Vascular) and is currently being tested in patients with peripheral vascular disease (ClinicalTrials.gov Identifier: NCT04227899). An iron-based resorbable scaffold (IBS) with 70 μm strut thickness has shown similar 1-year efficacy and safety as CoCr-EES in porcine coronary arteries.[20]

Between 3 and 5 years after randomization in the present study the rates of TLF and device thrombosis were similar with BVS and CoCr-EES, similar to that reported from a pooled experience from the four prior ABSORB randomized trials.[9] Notably the device-oriented outcome of TLF after 3 years occurred at a constant rate of 2.5% per year with both BVS and CoCr-EES. The modest numbers of events in this period and the truncated follow-up at 5 years precludes drawing firm conclusions as to whether the theoretical potential of BVS to reduce the ongoing long-term risk of adverse events common to all metallic stents will be realized.[1,2]

Cardiac and all-cause death rates at 5 years were similar after BVS and CoCr-EES. Angina also recurred with nearly identical frequency, a finding consistent with the results from prior studies demonstrating similar rates of angiographic restenosis,[3] myocardial blood flow and coronary flow reserve[21] after both devices. Nor were the SAQ or EuroQOL-5D scores meaningfully different between BVS and CoCr-EES. Thus, the long-term impact of BVS and

CoCr-EES on survival, patient-oriented outcomes and QoL in this trial were comparable. Notably, however, the comprehensive continuous assessment and adjudication of angina and anginal equivalent symptoms documented recurrent ischemic symptoms in ~53% of patients in both groups at some point during the 5-year follow-up. In contrast, eliciting the rate of angina symptoms present at discrete annual follow-up visits yielded rates of <10% at each time point, markedly under-estimating the symptomatic burden during the follow-up course. The 53% recurrence rate of adjudicated typical angina or anginal equivalent symptoms within 5 years is particularly striking given that ischemia-driven revascularization (of any vessel) was performed in only ~15% of patients. In some patients symptoms may have been transitory or mild, enabling medical management alone without repeat revascularization. Untreated diffuse coronary artery disease may also contribute to recurrent angina.[22] However, this disparity reinforces the increasing awareness that vasoreactivity and microvascular disease may strongly contribute to the chronic symptomatology of a large proportion of patients with obstructive epicardial coronary artery disease (as well as in patients with angina without obstructive disease).[23]

Limitations. ABSORB IV had less restrictive enrollment criteria than most prior trials. Nonetheless, many high-risk lesions were excluded, including severely calcified lesions, true bifurcation lesions, and chronic total occlusions. The characteristics of these lesions may favor metallic DES, although improved BVS design and more aggressive lesion preparation may narrow the differences. Conversely, some excluded patients and lesions such as those with acute ST-segment elevation MI (soft plaque) and left main disease (large RVD, short lesion length) may have favorable outcomes after BVS. As previously discussed, the use of intravascular imaging guidance was not strongly promoted; its routine use may be of particular benefit with BVS. The present results were not powered and so should be considered hypothesis generating.

Even larger studies with longer-term follow-up (e.g. 10 years) may be required to determine whether BVS reduce late events after 3 years compared with metallic DES, although even if not, if the long-term results are truly non-inferior, the other benefits of "leaving nothing behind" may be of utility in certain clinical scenarios and be preferred by some patients. Finally, the present results apply only to the first-generation Absorb BVS. As improved BVS emerge, they will require randomized comparison with best-in-class contemporary metallic DES with long-term follow-up.

Conclusions

In the present large-scale, blinded randomized trial, Absorb BVS implanted with improved lesion selection and technique in patients with both acute and chronic coronary syndromes resulted in slightly higher rates of TLF and device thrombosis within 3 years compared with CoCr-EES, with absolute increments in this period of 3% and 1% respectively. In contrast, the rates of these outcomes were nearly identical with both devices after 3 years. Both devices resulted in comparable 5-year rates of death, patient-oriented composite events and quality-of-life. Notably, more than half of patients developed recurrent anginal or anginal equivalent symptoms within 5 years at some time after PCI, a much greater symptom burden than is appreciated by simply assessing angina at discrete time points only. Further study is warranted to examine the extent to which microvascular disease and vasospasm contribute to the high rate of recurrent symptoms after PCI in patients with obstructive coronary artery disease.

Clinical Perspectives

Competency in Medical Knowledge: In the ABSORB-IV trial, implantation of the first generation polymeric everolimus-eluting bioresorbable vascular scaffold (BVS) with optimal technique in appropriately sized coronary arteries resulted in slightly increased rates of target lesion failure (TLF) and device thrombosis compared with metallic drug-eluting stents (DES) within the first 3 years prior to their complete bioresorption, but overall similar 5-year rates of death, patient-oriented composite events, angina recurrence and quality-of-life.

Competency in Patient Care: Angina recurred within 5 years after percutaneous coronary intervention (PCI) at some time in more than half of patients treated with either BVS or DES, although is reported in <10% of patients at any discrete time point, and often can be managed medically without revascularization.

Translational Outlook 1: Further studies are required to determine whether BVS with improved mechanical properties implanted with intravascular imaging will have comparable 3-year outcomes compared with metallic DES, with improved long-term event-free survival.

Translational Outlook 2: Additional studies are also required to evaluate the extent that microvascular disease and altered vasoreactivity contribute to the high recurrence rate of angina in patients with (and without) obstructive coronary artery disease after PCI.

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Figure Legends

Figure 1. Time-to-first event curves for 5-year TLF and its components.

A) Target lesion failure; B) Cardiac death; C) Target-vessel myocardial infarction; D) Ischemia-driven target lesion revascularization; E) Device thrombosis (definite or probable). BVS = Absorb bioresorbable vascular scaffolds. CoCr-EES = Xience cobalt chromium everolimus-eluting stents. MI = myocardial infarction. TLF = target lesion failure. TLR = target lesion revascularization.

Figure 2. Landmark analysis at 3 years for TLF and device thrombosis.

A) Target lesion failure; B) Device thrombosis (definite or probable). *In the landmark analysis, all patients still alive are included in the numbers at risk at 3 years, regardless of whether an event occurred before this time. The interaction p values for the comparison of the relative hazards for BVS vs. CoCr-EES between 0-3 years and 3-5 years were 0.046 and 0.11 for target lesion failure and device thrombosis respectively. BVS = Absorb bioresorbable vascular scaffolds. CoCr-EES = Xience cobalt chromium everolimus-eluting stents. TLF = target lesion failure.

Figure 3. Cumulative incidence of angina through 5-year follow-up.

Angina was defined as typical angina or angina equivalent symptoms as adjudicated by the clinical events committee. BVS = Absorb bioresorbable vascular scaffolds. CoCr-EES = Xience cobalt chromium everolimus-eluting stents.

Central Illustration. Principal 5-year results from the ABSORB IV trial.

Among 2406 patients randomized to the Absorb everolimus-eluting poly(L-lactide) bioresorbable vascular scaffold (BVS) or the Xience cobalt chromium everolimus-eluting stent (CoCr-EES), the 5-year rates of target lesion failure with BVS were increased by an absolute

difference of 3.0%, whereas there were no significant differences in the 5-year rates of device thrombosis. BVS was associated with higher event rates during the first 3 years after randomization, until the time of its complete bioresorption. Thereafter event rates were similar with BVS and CoCr-EES. Angina recurred in >50% of patients during the 5-year follow-up, to a comparable degree with both stents. The burden of recurrent angina was substantially under-estimated by only considering angina prevalence at discrete time points. Cum = cumulative through 5 years. y = year.

Table 1. Baseline clinical and angiographic characteristics of the randomized groups

Patient measures	**Absorb BVS (N=1296)**	**Xience CoCr-EES (N=1308)**
Age (years)	63.1 ± 10.1	62.2 ± 10.3
Sex (male)	927/1296 (71.5%)	947/1308 (72.4%)
Race/ethnicity (Caucasian)	1135/1296 (87.6%)	1160/1308 (88.7%)
Body mass index (kg/m^2)	30.3 ± 5.9	30.2 ± 6.1
Hypertension treated with medications	966/1296 (74.5%)	981/1308 (75.0%)
Dyslipidemia treated with medications	921/1296 (71.1%)	920/1307 (70.4%)
Diabetes mellitus	409/1296 (31.6%)	417/1306 (31.9%)
- Insulin-treated	150/1296 (11.6%)	145/1306 (11.1%)
Prior myocardial infarction	230/1279 (18.0%)	252/1297 (19.4%)
Current tobacco use	286/1294 (22.1%)	304/1306 (23.3%)
Renal insufficiency*	180/1294 (13.9%)	170/1306 (13.0%)
Clinical presentation		
- Stable CAD	983/1294 (76.0%)	997/1308 (76.2%)
- Silent ischemia or ischemia not documented	95/1294 (7.3%)	98/1308 (7.5%)
- Stable angina	661/1294 (51.1%)	670/1308 (51.2%)
- Unstable angina, biomarker negative	227/1294 (17.5%)	229/1308 (17.5%)
- Recent MI	311/1294 (24.0%)	311/1308 (23.8%)
- Non-ST-segment elevation MI	288/1294 (22.3%)	290/1308 (22.2%)
- ST-segment elevation MI	8/1294 (0.6%)	11/1308 (0.8%)
- Post-MI angina, MI type unspecified	15/1294 (1.2%)	10/1308 (0.8%)
Target vessel measures (core laboratory)	**V=1368**	**V=1382**
TIMI flow		

- 0/1	43/1362 (3.2%)	27/1377 (2.0%)
- 2	180/1362 (13.2%)	187/1377 (13.6%)
- 3	1139/1362 (83.6%)	1163/1377 (84.5%)
Target lesion measures (core laboratory)	**L=1446**	**L=1457**
Coronary artery location		
- Left anterior descending	629/1443 (43.6%)	635/1453 (43.7%)
- Left circumflex	374/1443 (25.9%)	376/1453 (25.9%)
- Right	440/1443 (30.5%)	442/1453 (30.4%)
ACC/AHA lesion class B2/C	677/1443 (46.9%)	663/1453 (45.6%)
Moderate or severe calcification	346/1438 (24.1%)	341/1451 (23.5%)
Moderate or severe tortuosity	125/1439 (8.7%)	109/1451 (7.5%)
Bifurcation	246/1425 (17.3%)	252/1442 (17.5%)
Reference vessel diameter (mm)	2.90 ± 0.39	2.89 ± 0.38
- <2.25 mm	36/1441 (2.5%)	42/1452 (2.9%)
Minimum luminal diameter (mm)	0.82 ± 0.35	0.81 ± 0.34
Diameter stenosis (%)	71.8 ± 11.2	71.8 ± 10.9
Lesion length (mm)	14.8 ± 6.2	15.1 ± 6.9

*Calculated glomerular filtration rate <30 mL/min/1.73m^2. BVS = bioresorbable vascular scaffolds. CoCr-EES = cobalt chromium everolimus-eluting stents. N = number of patients. L = number of target lesions. MI = myocardial infarction. TIMI = Thrombolysis in Myocardial Infarction. V = number of target lesions.

Table 2. Five-year clinical outcomes in the randomized groups

	Absorb BVS (N=1296)	Xience CoCr-EES (N=1308)	HR [95% CI]	P value
Target-lesion failure	216 (17.5%)	180 (14.5%)	1.24 [1.02, 1.52]	0.03
Cardiac death	30 (2.5%)	30 (2.5%)	1.02 [0.61, 1.69]	0.95
Target-vessel MI	134 (10.8%)	106 (8.5%)	1.30 [1.00, 1.67]	0.04
Ischemia-driven TLR	111 (9.2%)	82 (6.8%)	1.40 [1.05, 1.87]	0.02
Major adverse cardiovascular events	233 (18.9%)	207 (16.7%)	1.16 [0.97, 1.40]	0.11
Target vessel failure	262 (21.3%)	240 (19.3%)	1.13 [0.95, 1.35]	0.16
Patient-oriented composite endpoint	310 (25.0%)	284 (22.7%)	1.13 [0.96, 1.33]	0.13
All-cause death	77 (6.4%)	72 (5.9%)	1.09 [0.79, 1.50]	0.60
Vascular death	4 (0.3%)	6 (0.5%)	0.68 [0.19, 2.41]	0.55
Non-cardiovascular death	47 (4.0%)	42 (3.5%)	1.14 [0.75, 1.73]	0.54
All MI (protocol definition)	154 (12.5%)	134 (10.8%)	1.18 [0.93, 1.48]	0.16
Q-wave	20 (1.6%)	14 (1.2%)	1.46 [0.74, 2.88]	0.28
Non-Q-wave	139 (11.3%)	123 (9.9%)	1.16 [0.91, 1.47]	0.24
Peri-procedural	51 (4.0%)	45 (3.5%)	1.15 [0.77, 1.71]	0.50
Spontaneous	108 (8.9%)	92 (7.6%)	1.20 [0.91, 1.59]	0.19
All revascularization	198 (16.3%)	167 (13.7%)	1.23 [1.00, 1.51]	0.047
Ischemia-driven	197 (16.2%)	167 (13.7%)	1.22 [1.00, 1.50]	0.054
TVR	165 (13.6%)	131 (10.8%)	1.31 [1.04, 1.65]	0.02
Non-TVR	71 (5.9%)	82 (6.7%)	0.88 [0.64, 1.21]	0.43
Non-ischemia-driven	7 (0.6%)	3 (0.2%)	2.37 [0.61, 9.16]	0.20
Device thrombosis (definite/probable)	21 (1.7%)	13 (1.1%)	1.65 [0.82, 3.29]	0.15
Definite	20 (1.6%)	13 (1.1%)	1.57 [0.78, 3.15]	0.20

Probable	1 (0.1%)	0 (0.0%)	-	0.32
Early (≤30 days)	8 (0.6%)	2 (0.2%)	4.05 [0.86, 19.06]	0.06
Late (31 days – 1 year)	1 (0.1%)	2 (0.2%)	0.51 [0.05, 5.59]	0.57
Very late (1 year – 5 years)	12 (1.0%)	10 (0.8%)	1.23 [0.53, 2.84]	0.63

Data are number of events (Kaplan-Meier estimated rates). BVS = bioresorbable vascular scaffolds. CoCr-EES = cobalt chromium everolimus-eluting stents. MI = myocardial infarction. MI = myocardial infarction. TLR = target lesion revascularization. TVR = target vessel revascularization. Major adverse cardiovascular events are the composite of cardiac death, all myocardial infarction, or ischemia-driven target lesion revascularization. The patient-oriented composite endpoint is the composite of all death, all myocardial infarction, or all revascularization. Target lesion failure is the composite of cardiac death, myocardial infarction attributable to the target vessel, or ischemia-driven target lesion revascularization. Target vessel failure is the composite of cardiac death, all myocardial infarction, or ischemia-driven target vessel revascularization.

Table 3. Cumulative angina recurrence through 5-year follow-up

	Absorb BVS (N=1296)	Xience CoCr-EES (N=1308)	HR (95% CI)	P value
From randomization through 5 years				
Angina	452 (36.3%)	473 (37.5%)	0.95 [0.84, 1.08]	0.44
Class I*	188 (15.2%)	185 (14.8%)	1.03 [0.84, 1.26]	0.76
Class II*	211 (17.1%)	220 (17.5%)	0.96 [0.80, 1.16]	0.69
Class III*	137 (11.2%)	162 (13.0%)	0.85 [0.67, 1.06]	0.15
Class IV*	105 (8.5%)	100 (7.9%)	1.06 [0.81, 1.40]	0.66
Anginal equivalent symptoms	357 (29.0%)	357 (28.4%)	1.01 [0.87, 1.17]	0.89
Class I*	50 (4.0%)	58 (4.6%)	0.87 [0.60, 1.27]	0.47
Class II*	200 (16.3%)	193 (15.5%)	1.06 [0.87, 1.29]	0.57
Class III*	178 (14.6%)	181 (14.5%)	0.99 [0.81, 1.22]	0.95
Class IV*	39 (3.2%)	36 (2.9%)	1.10 [0.70, 1.73]	0.68
Angina or anginal equivalent symptoms	659 (53.0%)	674 (53.3%)	0.97 [0.88, 1.08]	0.63
Class I*	233 (18.9%)	228 (18.2%)	1.04 [0.87, 1.25]	0.69
Class II*	369 (29.9%)	377 (30.0%)	0.99 [0.86, 1.14]	0.86
Class III*	275 (22.3%)	307 (24.5%)	0.89 [0.76, 1.05]	0.16
Class IV*	136 (11.0%)	129 (10.3%)	1.07 [0.84, 1.36]	0.60
Landmark analyses				
Between 0 and 1 year	463 (36.3%)	497 (38.6%)	0.93 [0.82, 1.05]	0.23
Between 1 and 2 years*	197 (16.2%)	172 (13.9%)	1.19 [0.97, 1.46]	0.10
Between 2 and 3 years*	169 (14.2%)	171 (14.1%)	1.02 [0.82, 1.26]	0.86
Between 3 and 4 years*	154 (13.4%)	127 (10.8%)	1.26 [1.00, 1.60]	0.05
Between 4 and 5 years*	139 (12.5%)	117 (10.3%)	1.23 [0.96, 1.57]	0.10

Non-anginal symptoms	743 (59.6%)	711 (56.1%)	1.09 [0.98, 1.21]	0.11

Event rates are number of events (Kaplan-Meier estimated rates). In-hospital symptoms are excluded. *Symptoms of this class reported anytime within 5 years. Thus, the total may add up to >100%. BVS = bioresorbable vascular scaffolds. CoCr-EES = everolimus-eluting stents.

Table 4. Recurrent angina at each follow-up visit

	Absorb BVS (N=1296)	Xience CoCr-EES (N=1308)	P value
At 1 year (365 ± 28 days)	N=1203	N=1224	
Angina	28 (2.3%)	36 (2.9%)	0.35
Anginal equivalent symptoms	86 (7.1%)	70 (5.7%)	0.15
Angina or anginal equivalent symptoms	114 (9.5%)	105 (8.6%)	0.44
Class I	23 (1.9%)	16 (1.3%)	0.24
Class II	48 (4.0%)	44 (3.6%)	0.61
Class III	35 (2.9%)	45 (3.7%)	0.29
Class IV	8 (0.7%)	7 (0.6%)	0.77
Non-anginal symptoms	101 (8.4%)	126 (10.3%)	0.11
At 2 years (730 ± 28 days)	N=1162	N=1186	
Angina	35 (3.0%)	25 (2.1%)	0.17
Anginal equivalent symptoms	77 (6.6%)	73 (6.2%)	0.64
Angina or anginal equivalent symptoms	112 (9.6%)	97 (8.2%)	0.21
Class I	20 (1.7%)	14 (1.2%)	0.27
Class II	46 (4.0%)	44 (3.7%)	0.75
Class III	39 (3.4%)	32 (2.7%)	0.35
Class IV	9 (0.8%)	8 (0.7%)	0.78
Non-anginal symptoms	91 (7.8%)	94 (7.9%)	0.93
At 3 years (1095 ± 28 days)	N=1129	N=1162	
Angina	23 (2.0%)	22 (1.9%)	0.80
Anginal equivalent symptoms	79 (7.0%)	70 (6.0%)	0.34
Angina or anginal equivalent symptoms	100 (8.9%)	91 (7.8%)	0.37

Class I	12 (1.1%)	11 (0.9%)	0.78
Class II	45 (4.0%)	37 (3.2%)	0.30
Class III	35 (3.1%)	34 (2.9%)	0.81
Class IV	10 (0.9%)	10 (0.9%)	0.95
Non-anginal symptoms	92 (8.1%)	99 (8.5%)	0.75
At 4 years (1460 ± 28 days)	N=1133	N=1132	
Angina	22 (1.9%)	12 (1.1%)	0.08
Anginal equivalent symptoms	67 (5.9%)	56 (4.9%)	0.31
Angina or anginal equivalent symptoms	89 (7.9%)	68 (6.0%)	0.08
Class I	12 (1.1%)	8 (0.7%)	0.37
Class II	27 (2.4%)	24 (2.1%)	0.67
Class III	38 (3.4%)	31 (2.7%)	0.39
Class IV	12 (1.1%)	5 (0.4%)	0.09
Non-anginal symptoms	74 (6.5%)	75 (6.6%)	0.93
At 5 years (1825 ± 28 days)	N=1110	N=1128	
Angina	7 (0.6%)	7 (0.6%)	0.98
Anginal equivalent symptoms	73 (6.6%)	60 (5.3%)	0.21
Angina or anginal equivalent symptoms	80 (7.2%)	67 (5.9%)	0.23
Class I	3 (0.3%)	7 (0.6%)	0.34
Class II	35 (3.2%)	17 (1.5%)	0.01
Class III	37 (3.3%)	39 (3.5%)	0.87
Class IV	5 (0.5%)	4 (0.4%)	0.75
Non-anginal symptoms	83 (7.5%)	66 (5.9%)	0.12

Rates at each time point are binary data. BVS = bioresorbable vascular scaffolds. CoCr-EES = cobalt chromium everolimus-eluting stents.