

SUPPLEMENTARY DATA

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

Table S1. Schedule of visits and data assessment throughout the study

Type of contact	Selection (Visit)	PCI (Visit)	Post-PCI discharge (Visit)	1 month after PCI (± 3 days) (Phone)	6 months after PCI (± 3 days) (Phone)	9 months after PCI (± 30 days)	12 months after PCI (± 45 days) (Phone)	24 months after PCI (± 45 days) (Phone)
Inclusion/Exclusion criteria	X							
Informed consent	X							
Vital signs	X							
Medical history	X							
Angina/Vital status	X		X	X	X	X	X	X
12-lead ECG	X		X			X		
LVEF (by echocardiography)	X							
Coronary angiography	X	X				X		
OCT		X				If clinically indicated		
Antithrombotic medication	X		X	X	X	X	X	X
Serious adverse event reporting	X	X	X	X	X	X	X	X

ECG, electrocardiogram; LVEF, left ventricular ejection fraction; OCT, optical coherence tomography; PCI, percutaneous coronary intervention.

Appendix S1. Variable and endpoints definitions

- **Calcified nodule (CN)**: defined as a calcified segment with an accumulation of nodular calcification (small calcium deposits) with disruption of the fibrous cap (eruptive CN) or an intact thick fibrous cap (non-eruptive CN).
- **Late lumen loss (LLL)**: according to the Drug Coated Balloon Academic Research Consortium consensus document.¹ Difference between post-procedural and follow-up minimal lumen diameter (MLD)
- **Net gain**¹: difference between follow-up and pre-procedural MLD
- **Binary restenosis**¹: luminal diameter reduction of $\geq 50\%$ at follow-up.
- **Cross-over**: change of intended pre-specified procedural strategy to another (drug eluting balloon [DEB] to drug eluting stent [DES] or DES to DEB)
- **Angiographic success**: final stenosis $< 30\%$ in the DEB arm and $< 20\%$ in the DES arm, with no flow-limiting \geq type C dissections (final flow TIMI 3). This difference in the percentage of final stenosis is due to the intrinsic difference between a stent and a DEB, which is more prone to acute recoil due to the absence of scaffolding properties.
- **Device success**: defined as angiographic success without crossover between treatment arms.
- **Procedural success**: angiographic success and absence of procedural and in-hospital cardiovascular complications.
- **Major adverse cardiovascular event (MACE)**: composite of cardiac death, myocardial infarction (MI) related to the treated lesion, target lesion revascularization [TLR]).
- **Stent Expansion Percentage**: defined as the ratio of the minimum luminal area of the stent divided by the mean of the minimum luminal areas of the proximal and distal reference vessel.
- **Death of cardiovascular origin**: According to ARC (Academic Research Consortium) definitions²: any death due to a known cardiac cause such as AMI, arrhythmia or heart failure, unexpected death or death of unknown cause. Procedure-related death and death related to cardiac pathology treatments are included. Also included is death from vascular causes not due to coronary artery disease such as stroke, aortic dissection, pulmonary embolism or vascular disease.
- **Non-fatal AMI**: According to the fourth universal definition of AMI, with or without ST-segment elevation.³ A distinction is made between those associated with the procedure (occurring within 48 hours of the procedure) and "spontaneous" (occurring > 48 hours after the procedure) and those related to the target lesion or not.
- **Types of coronary dissection**:
 - Type-A: radiolucent area in the coronary lumen with minimal or no contrast persistence.
 - Type-B: double parallel lumen separated by a radiolucent area with minimal or no contrast persistence.
 - Type C: persistent presence of contrast outside the coronary lumen.
 - Type-D: Spiroid luminal contrast defect.
 - Type-E: dissection with persistent contrast defect.
 - Type-F: dissection with total coronary occlusion.

- **Stent thrombosis according to ARC**²
 - Definitive: Confirmed angiographically (TIMI 0 or thrombus image) + clinical, electrical or biological (enzymatic elevation) evidence of acute ischemia or thrombosis demonstrated by pathological anatomy.
 - Probable: unexplained death in the first 30 days of follow-up or AMI in implanted stent territory.
 - Possible: Unexplained death 30 days after stent implantation.
- **Stroke**: New focal neurological deficit assessed by imaging and confirmed by neurology.
- **Target lesion revascularization (TLR)**²: That previously treated with stent included 5 mm proximal and distal to the stent. By definition, it should also be reported as target vessel revascularization.
- **Target vessel revascularization (TVR)**²: New lesion in the treated vessel during the index event, unrelated to previously treated lesion or related to it.
- **Moderately calcified lesion**: radiopacities visible only during the cardiac cycle and typically only on one side of the vascular wall.
- **Severely calcified lesion**:
 - Angiographically: radiopacities visible without cardiac motion before contrast injection and generally affecting both sides of the vessel.
 - Intracoronary imaging: > 180° calcium arc or calcium plaques with depth >5 mm.
- **Bleeding BARC** (Bleeding Academic Research Consortium)⁴:
 - Type 0: no bleeding.
 - Type 1: bleeding without practical repercussions that does not require studies, hospitalization or unscheduled treatment; it may include episodes that cause the patient to discontinue medical treatment without consulting health professionals.
 - Type 2: any sign of relevant bleeding (more bleeding than expected from the clinical picture; including non-clinical bleeding, only detectable by imaging techniques) that does not fit into the above categories BUT meets any of the following criteria:
 - Need for medical intervention, not surgical
 - Need for hospitalization or increased level of care
 - Need for further evaluation.
 - Type 3
 - Type 3a
 - Overt bleeding with hemoglobin drop of 3 to 5

- Type 3b
 - Overt bleeding with hemoglobin drop of ≥ 5
 - Cardiac tamponade
 - Bleeding requiring surgical intervention for control (excluding dental / nasal / skin / hemorrhoids)
 - Bleeding requiring intravenous infusion of vasoactive agents.
- Type 3c
 - Intracranial hemorrhage (including intraspinal, not including microbleeds or hemorrhagic transformation)
 - Subcategories confirmed by necropsy, imaging technique or lumbar puncture
 - Intraocular bleeding that compromises vision
- Type 4: Bleeding related to coronary surgery.
 - Perioperative intracranial hemorrhage (in the first 48 hours)
 - Reoperation after sternotomy closure for bleeding control
 - Transfusion of ≥ 5 Units of blood or red cells in a 48 hour period
 - Collection of ≥ 2 L by thoracic drainage in a 24 hour period.
- Type 5: Fatal bleeding
 - Type 5a: Death of probable hemorrhagic origin due to clinical suspicion, without confirmation by autopsy or imaging test.
 - Type 5b: Death of definite hemorrhagic origin, with evident bleeding or confirmation by necropsy or imaging test.
- **Angiographic success:** Final TIMI 3 flow and residual stenosis $<20\%$ (additional thresholds of 30% and 50% will also be evaluated).
- **Procedural success:** Angiographic success without major procedure-related complications (death, perforation, acute vessel closure, flow-limiting dissection or BARC bleeding $\geq 3b$).
- **Strategy success:** Procedural success without the need for crossover.
- **Clinical success:** Procedural success without major in-hospital complications (death, TLR, definite or probable stent thrombosis, or stroke).

Supplementary references

1. Fezzi S, Scheller B, Cortese B, et al. Definitions and standardized endpoints for the use of drug-coated balloon in coronary artery disease: consensus document of the Drug Coated Balloon Academic Research Consortium. *EuroIntervention*. Published online April 2025. doi:10.4244/EIJ-E-25-00021.
2. Garcia-Garcia HM, McFadden EP, Farb A, et al. Standardized End Point Definitions for Coronary Intervention Trials: The Academic Research Consortium-2 Consensus Document. *Circulation*. 2018;137(24):2635-2650. doi:10.1161/circulationaha.117.029289.
3. Thygesen K, Alpert JS, Jaffe AS, et al. Fourth Universal Definition of Myocardial Infarction (2018). *Circulation*. 2018;138(20). doi:10.1161/cir.0000000000000617
4. Mehran R, Rao SV, Bhatt DL, et al. Standardized Bleeding Definitions for Cardiovascular Clinical Trials: A Consensus Report From the Bleeding Academic Research Consortium. *Circulation*. 2011;123(23):2736-2747. doi:10.1161/CIRCULATIONAHA.110.009449