Supplementary data

Supplementary Appendix 1. ISAR-CALC trial committees

- **Steering committee**: Robert A. Byrne (Chair); Salvatore Cassese (Principal Investigator); Michael Joner (Sub-Principal Investigator); Mohamed Abdel-Wahab (Sub-Principal Investigator).
- **Clinical project manager**: Tobias Rheude.
- **Clinical event adjudication committee**: Gjin Ndrepepa (Chair); Andreas Stein; Giulio Stefanini.
- **Patient follow-up and data coordination at the *ISAResearch Center, Munich, Germany***: Stefanie Brunner, Nonglag Rifatov, Felix Voll, Barbara von Merzljak, Jens Wiebe.
- **Angiographic and intravascular imaging core laboratory at the *ISAResearch Center, Munich, Germany***: Susanne Pinieck, Silvia Hurt (quantitative angiographic core laboratory analysis), Himanshu Rai, Erion Xhepa (optical coherence tomography core laboratory analysis).

Contract research organisation for independent data monitoring and audit: KCRI, Krakow, Poland.

Supplementary Appendix 2. Protocol for acquisition and analysis of quantitative coronary angiography data

Coronary angiograms were digitally recorded, stored offline and analysed by independent personnel unaware of treatment allocation in the quantitative coronary angiographic (QCA) core laboratory (ISAResearch Center, Munich, Germany) using an automated edge detection system (QAngio XA version 7.3; Medis Medical Imaging Systems, Leiden, the Netherlands) and a predefined standard operating procedure. The analysis was based on digitisation of coronary angiograms, image calibration and arterial automatic contour detection, as previously described. At least a 6 Fr guiding catheter with good support and co-axial alignment was requested for all coronary angiograms. A baseline angiography of the target vessel with and without contrast (filled/empty, approximately 3-4 cardiac cycles) served for quantification of coronary calcium at the level of the target lesion and qualitative evaluation of baseline angiographic features. During the acquisition, a minimum of 3 cm of the non-tapered distal, dye-filled catheter should be visible for calibration purposes. Baseline coronary angiograms were selected before guidewire advancement to avoid artefacts. Baseline QCA measures comprised, but were not limited to, minimal luminal diameter (MLD, the smallest lumen diameter in the segment of interest), reference vessel diameter (RVD, the averaged diameter of the coronary assumed without atherosclerotic disease), lesion length (length of the stenosis as measured by two points where the coronary margins change direction, creating a shoulder between the angiographically normal sub-segment and the diseased sub-segment), and diameter stenosis ([RVD-MLD]/RVD*100). The failure of lesion preparation with a standard non-compliant balloon at maximal pressure was recorded and documented in the intervention protocol transmitted for all patients enrolled for source verification. For evaluation of acute luminal gain (MLD after balloon angioplasty with the study devices minus baseline MLD), the coronary angiograms with study balloon inflation (at maximal pressure) were recorded and the sequence was indicated in the intervention protocol (omitting any information regarding the type of device used). After lesion preparation with the assigned study device, any other device used for complementary lesion preparation was recorded (standard non-compliant balloon at maximal pressure or any rotablation run, if necessary) and documented in the intervention protocol for source verification. For the stent implantation, the stent-balloon inflation (at maximal pressure) was recorded. Baseline QCA measurements were performed using the coronary angiograms with the single worst view projection of the target lesion; the same view projection was used for measurements after intervention. Final angiographic results were measured before OCT pullback (performed for the assessment of the primary endpoint) or after OCT pullback and guidewire removal in case of no additional coronary interventions. Pre- and post-PCI coronary angiograms were obtained at the same magnification and the same view projection. All measurements were performed on coronary angiograms recorded after the intracoronary administration of nitroglycerine (200 mcg).

Protocol for acquisition and analysis of OCT data

OCT pullbacks were stored offline and analysed using Windows-based QIvus 3.1.12.0 software (Medis Medical Imaging Systems) by independent personnel unaware of treatment allocation in the imaging core laboratory (ISAResearch Center, Munich, Germany) using a predefined standard operating procedure. At least a 6 Fr guiding catheter (ideally without side

holes) with good support and co-axial alignment was requested for all OCT pullbacks. After infusion of intracoronary nitroglycerine (200 mcg) and after ensuring that the OCT catheter lumen was purged by injection of at least 1-2 ml of pure contrast, the OCT catheter was advanced into the target vessel such that the scanning crystal lay ca. 10 mm distal to the distal stent edge and such that the end of the pullback was 10 mm proximal to the proximal stent edge. In case of long lesions, more than one OCT pullback was permitted. The automatic pullback was started while 20 ml of contrast was infused at a rate of 5 ml/s (left coronary artery) or 16 ml of contrast at a rate of 4 ml/s (right coronary artery). The unitary acquisition length for OCT pullbacks was 75 mm or 54 mm, the axial scanning rate was 100 Hz and the rate of pullback acquisition was 36 mm/s or 18 mm/s. Morphometric analysis of contiguous cross-sections within the stented segment was performed for each 1 mm longitudinal interval. Software-aided automatic strut detection was performed, adjusted in case of anomalies and later connected to identify stent contour. Stent area in each analysed frame was defined as the circumferential area limited by the stent contour. In frames with stent overlap and visible strut crowding, the layer of stent struts closest to the vessel's endoluminal surface was used to extrapolate the stent contour. Software-aided automatic lumen contour detection was performed within 5 mm from the distal and proximal stent edge (reference segments) in order to identify proximal and distal reference lumen areas. Reference lumen area is defined as a representative, preferably disease-free, frame contained within the reference segment. Mean reference lumen area was calculated using the following formula: (distal reference lumen area + proximal reference lumen area) / 2. If the pullback lacked analysable reference segments, the proximal or distal reference area was extrapolated from the most analysable proximal or distal stent area. To account for natural vessel tapering in case of long lesions (>70 mm), stented segments were split into two equal segments and analysed separately. In the case of long lesions requiring two or more OCT pullbacks for the stented segment, anatomical landmarks (e.g., side branches) were used as bookmarks for splitting the analysis. Additional coronary interventions following OCT imaging were permitted in case of evidence of suboptimal procedural results (i.e., residual dissection) at the discretion of the operator. In addition, further OCT pullbacks were allowed at the operator's discretion without being considered for primary endpoint evaluation.

Supplementary Table 1. Inclusion/exclusion criteria of the ISAR-CALC trial.

Inclusion criteria
- Age above 18 years and consentable - Persistent angina despite optimal medical therapy and/or evidence of inducible ischaemia - Angiographically proven coronary artery disease - De novo lesion in a native coronary artery - Target reference vessel diameter between 2.25 and 4.00 mm by visual estimation - Severe calcification of the target lesion as determined by visual estimation at coronary angiography - Unsuccessful lesion preparation with standard non-compliant balloon (<30% reduction of baseline diameter stenosis at maximal pressure) - Written informed consent.
Exclusion criteria
- Myocardial infarction (within 1 week) - Target lesion is located in a coronary artery bypass graft - Target lesion is an in-stent restenosis - Target lesion is aorto-ostial - Target vessel thrombus - Limited long-term prognosis due to other comorbid conditions.

Supplementary Table 2. Cumulative 30-day clinical outcomes.

	Super high-pressure balloon (n=37)	Scoring balloon (n=37)	*p*-value
MACE	-	10.8% (4/37)	0.11
Cardiac death	-	0	-
Target vessel myocardial infarction	-	5.4% (2/37)	0.49
Repeat revascularisation	-	8.1% (3/37)	0.24