

Abluminus DES+ sirolimus-eluting stent versus everolimus-eluting stent in patients with diabetes and coronary artery disease (ABILITY Diabetes Global): results from a multicentre, randomised controlled trial



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Summary

Background In patients with coronary artery disease, diabetes increases the risk of restenosis and adverse cardiovascular events after percutaneous coronary intervention (PCI). The Abluminus DES+ is a thin-strut cobalt–chromium sirolimus-eluting stent (SES) with abluminal and balloon-surface coating intended to enhance drug delivery to the vessel wall. We aimed to compare the efficacy and safety of the Abluminus DES+ SES versus the XIENCE durable-polymer everolimus-eluting stent (EES) in patients with diabetes undergoing PCI.

Methods ABILITY Diabetes Global was a multicentre, prospective, open-label, randomised controlled trial conducted at 74 sites in 16 countries. Adults (aged ≥18 years) with type 1 or type 2 diabetes undergoing PCI for at least one de novo coronary lesion due to chronic coronary syndrome or non-ST-elevation acute coronary syndrome were eligible. Patients were randomly assigned (1:1) to the Abluminus DES+ SES or the XIENCE EES. Randomisation was stratified by site using a secure web-based system with concealed allocation and randomly varying block sizes (4, 6, and 8). Operators were unmasked to allocation; staff performing clinical follow-up and the independent clinical events committee were masked. For the Abluminus DES+ SES, a balloon inflation time of at least 45 s was recommended to facilitate drug transfer; dual antiplatelet therapy was prescribed to all patients according to clinical guidelines and local practice. The primary hypothesis of the study was the non-inferiority of the Abluminus DES+ SES compared with the XIENCE EES for the two coprimary endpoints at 12 months (in the per-protocol population): ischaemia-driven target-lesion revascularisation (2·8% non-inferiority margin) and target-lesion failure (3·0% margin), defined as a composite of cardiovascular death, target-vessel myocardial infarction, or ischaemia-driven target-lesion revascularisation. Time-to-event analyses were conducted with Kaplan–Meier estimates and Cox proportional hazards models. This trial is registered with ClinicalTrials.gov (NCT04236609) and is complete.

Findings Between June 12, 2020, and Sept 9, 2022, 3032 patients were randomly assigned to the Abluminus DES+ SES (n=1514) or XIENCE EES (n=1518). 2931 (96·7%) of 3032 patients completed follow-up to death or 24-month follow-up. Median age was 68·0 years (IQR 60–74). 879 (29·0%) of 3032 patients were female and 2153 (71·0%) were male. At 12 months, in the per-protocol analysis, the Abluminus DES+ SES did not meet the criteria for non-inferiority for ischaemia-driven target-lesion revascularisation compared with XIENCE EES (67 of 1421 patients [Kaplan–Meier estimate 4·8%, 95% CI 3·9–6·2] vs 30 of 1446 [2·1%, 95% CI 1·6–3·2]; absolute risk difference 2·7%, 95% CI 1·3–4·1; $p_{\text{non-inferiority}}=0·44$) and target lesion failure (137 [9·7%, 8·4–11·5] vs 89 [6·2%, 5·3–7·8]; 3·5%, 1·5–5·5; $p_{\text{non-inferiority}}=0·68$). For both endpoints, the lower bound of the 95% CI for the absolute risk difference excluded zero. Target-vessel myocardial infarction occurred more frequently in the Abluminus DES+ SES group (73 of 1421 patients [Kaplan–Meier estimate 5·2%, 95% CI 4·1–6·5] vs 44 of 1446 patients [3·1%, 2·4–4·3]) but there were no significant differences in cardiovascular death (41 of 1421 patients [2·9%, 2·1–3·9] vs 30 of 1446 patients [2·1%, 1·5–3·0]) and all-cause death (52 of 1421 patients [3·7%, 2·8–4·8] vs 48 of 1446 patients [3·3%, 2·5–4·4]). Results were consistent at 24 months in the intention-to-treat analysis, however no significant differences were observed between the two groups in landmark analyses between 12 and 24 months.

Interpretation In patients with diabetes undergoing PCI, the Abluminus DES+ SES was not non-inferior to the XIENCE EES, resulting in higher rates of ischaemia-driven target-lesion revascularisation and target lesion failure at 12-month follow-up. Event rates between 12 and 24 months were similar between groups. These findings highlight the persistent challenge of optimising outcomes in patients with diabetes and underscore the need for continued innovation in stent design and adjunctive pharmacotherapy to reduce residual ischaemic risk in this population.

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Introduction

Diabetes is a growing global health challenge, affecting more than 500 million individuals worldwide—a number that is projected to rise substantially over the coming decades.¹ Cardiovascular disease remains the leading cause of morbidity and mortality in patients with diabetes, with coronary artery disease often presenting with a more aggressive and diffuse pattern of atherosclerosis in these patients than in individuals without diabetes.² Hyperglycaemia, insulin resistance, and associated metabolic disturbances promote endothelial dysfunction, oxidative stress, and platelet hyperreactivity, facilitating pro-inflammatory and prothrombotic pathways.³ When myocardial revascularisation is required, patients with diabetes have a higher risk of major adverse cardiovascular events and repeat revascularisations.⁴ The FREEDOM trial⁵ showed that coronary artery bypass grafting provides better outcomes than percutaneous coronary intervention (PCI) in patients with diabetes and multivessel disease, particularly with respect to rates of death and myocardial infarction. However, a substantial proportion of patients with diabetes still require PCI due to anatomical suitability, high risk of adverse outcomes from surgery, or patient preference.⁶ In general, in patients with diabetes, outcomes after PCI remain suboptimal, especially because the mechanisms driving failure and in-stent restenosis are complex and include patient-related (eg, diffuse disease and vessel calibre), metabolic (eg, advanced glycation and endothelial dysfunction), and stent-related (eg, strut thickness, polymer biocompatibility, and drug resistance) factors.^{7–9} Although new-generation

drug-eluting stents (DESs) have outperformed bare-metal stents and first-generation DESs in all-comer patient cohorts, improvements in long-term clinical outcomes for patients with diabetes have been scarce.^{10–12}

The Abluminus DES+ (Concept Medical, Tampa, FL, USA) is a novel, thin-strut, cobalt–chromium sirolimus-eluting stent (SES) platform specifically designed for patients with diabetes.^{13,14} The anti-proliferative agent sirolimus is eluted from a biodegradable polymer matrix on the abluminal surface of the stent and exposed parts of the delivery balloon (hence the term DES+). This technology is intended to ensure uniform drug delivery within the lesions and stent edges, addressing the risk of restenosis while guaranteeing adequate re-endothelialisation.

The ABILITY Diabetes Global study aimed to compare the efficacy and safety of the Abluminus DES+ with the established durable-polymer everolimus-eluting XIENCE stent (Abbott, Santa Clara, CA, USA) in a large cohort of patients with diabetes undergoing PCI.

Methods

Study design and participants

ABILITY Diabetes Global was an international, multicentre, prospective, open-label, parallel-group, randomised clinical trial conducted at 74 sites across 16 countries in Europe, South America, and Asia. The full trial protocol is available in the appendix (pp 32–99). Details on participating sites, enrolment, and the ethical approvals obtained at each participating site from the respective local ethics committees are also provided in the appendix (pp 4–10).

Research in context

Evidence before this study

We searched PubMed, Embase, and major cardiology meeting proceedings from database inception to Aug 31, 2025, without language restrictions, using the terms “diabetes”, “drug-eluting stents”, “PCI”, and “randomized clinical trial”. Previous randomised trials and meta-analyses consistently showed that patients with diabetes have higher rates of restenosis and repeat revascularisation than patients without diabetes, despite improvements in new-generation drug-eluting stents (DES). Small mechanistic studies and observational studies of the Abluminus DES+ suggested feasibility and safety, but clinical evidence from large-scale randomised trials was absent.

Added value of this study

The ABILITY Diabetes Global trial is the largest randomised study to date focused exclusively on patients with diabetes undergoing percutaneous coronary intervention and showed that the Abluminus DES+ sirolimus-eluting stent did not meet criteria for non-inferiority compared with the XIENCE everolimus-eluting stent for ischaemia-driven target lesion

revascularisation and target lesion failure. The excess risk with the Abluminus DES+ was confined to the first year, driven by higher rates of target-vessel myocardial infarction and revascularisation, whereas outcomes were similar thereafter. This trial provides definitive, large-scale comparative data for two contemporary stent platforms in this high-risk population.

Implications of all the available evidence

Patients with diabetes remain at high risk of adverse events after percutaneous coronary intervention. The absence of an incremental benefit with the Abluminus DES+ highlights the ongoing unmet need for innovation in stent technology and adjunctive therapies to reduce residual ischaemic risk in patients with diabetes and coronary artery disease requiring percutaneous coronary intervention. Future research should explore device designs and pharmacological strategies that specifically address the biological challenges of diabetes. When feasible, surgical revascularisation should remain the preferred option for patients with diabetes and multivessel disease.

Patients aged 18 years or older with either a previously documented diagnosis of type 1 or type 2 diabetes and receiving pharmacological treatment, or a new diagnosis of diabetes irrespective of treatment status, were eligible. Patients had to be candidates for PCI for coronary artery disease presenting as chronic stable angina, silent ischaemia, or non-ST-elevation acute coronary syndrome. The angiographic inclusion criteria were the presence, by visual estimate, of at least one de novo coronary artery stenosis greater than 50% in a native coronary artery amenable to treatment with one or more stents (reference vessel diameter 2.25–4.0 mm; appendix p 11). Key clinical exclusion criteria comprised patients undergoing PCI for ST-elevation myocardial infarction, cardiogenic shock, known allergy to study stent drug or protocol required medications, planned surgery requiring dual antiplatelet therapy discontinuation within 6 months after the index procedure, acute or chronic renal dysfunction (defined as serum concentration of creatinine >3.0 mg/dL), and life expectancy less than 12 months; angiographic exclusion criteria were in-stent restenosis or lesions involving a bypass graft. The full list of exclusion criteria is provided in the appendix (p 12). All patients provided written informed consent, and the study was conducted in accordance with the principles of the Declaration of Helsinki. This trial is registered with ClinicalTrials.gov (NCT04236609) and is complete.

Randomisation and masking

Patients with diabetes deemed clinically eligible and suitable for treatment with PCI were considered for enrolment. After written informed consent was obtained, patients proceeded to the cardiac catheterisation laboratory for verification of angiographic inclusion and exclusion criteria. If all eligibility criteria were met, randomisation was performed after successful guidewire crossing and lesion predilatation. Patients were randomly assigned (1:1) to receive the Abluminus DES+ SES or the XIENCE everolimus-eluting stent (EES). The randomisation sequence was computer-generated using a permuted block design with randomly varying block sizes of 4, 6, and 8, stratified by investigational site, and used a secure web-based system with concealed allocation.

Operators were aware of the assigned study device; however, randomisation and device details were redacted from procedural reports and clinical documentation. Follow-up assessment was performed by research and clinical staff masked to treatment allocation, and all clinical events were adjudicated by an independent Clinical Events Committee (CEC) composed of experienced interventional and clinical cardiologists, neurologists, and critical care specialists that remained masked to study assignment.

Procedures

Stent implantation was performed in accordance with the instructions for use. For the Abluminus DES+ SES,

an inflation of at least 45 s was recommended to allow adequate drug delivery from the balloon to the vessel wall. There were no restrictions on the number of treated lesions, number of vessels, or lesion length, and procedural strategy was left to the operator's discretion. However, all lesions within a patient were to be treated using the assigned study device; staged procedures were permitted within 45 days after the index procedure and the same allocated device had to be used. Post-procedural management was at the discretion of the treating team, and dual antiplatelet therapy (consisting of aspirin plus a P2Y₁₂ inhibitor) was prescribed in accordance with current guideline recommendations and local practice.

Follow-up visits were scheduled at 1, 6, 12, and 24 months after randomisation. The 12-month visit was performed in person; the other follow-up visits could be conducted either in person or by telephone. At each visit, cardiovascular and diabetes-related medications and HbA_{1c} concentrations were recorded; the 12-month visit also included angina assessment, physical examination, 12-lead electrocardiogram (ECG), and standard laboratory testing. Criteria for patients to be removed from the study were withdrawal of consent, protocol violation precluding continued participation, or loss to follow-up.

Outcomes

The trial had two coprimary efficacy endpoints: (1) ischaemia-driven target lesion revascularisation (defined according to the Academic Research Consortium-2 criteria as any repeat percutaneous or surgical revascularisation of the target lesion [treated segment including 5 mm proximal and distal margins] in the presence of clinical or objective evidence of ischaemia),¹⁵ and (2) target lesion failure (defined as a composite of cardiovascular death, target-vessel myocardial infarction, or ischaemia-driven target lesion revascularisation), at 12 months, in the per-protocol population. The key secondary endpoint was a composite of cardiovascular death or target-vessel myocardial infarction. Other secondary clinical endpoints were the individual components of the coprimary endpoints, all-cause mortality, stent thrombosis, stroke, non-target lesions revascularisation target-vessel revascularisation, Bleeding Academic Research Consortium type 2 or greater bleeding, and stent thrombosis. Evidence of ischaemia was defined as symptoms of angina, abnormal ECG findings, a positive non-invasive functional test, or one of the following hierarchical criteria: (1) core laboratory fractional flow reserve of 0.80 or less or instant wave-free ratio of 0.89 or less; (2) site-reported fractional flow reserve of 0.80 or less or instant wave-free ratio of 0.89 or less; (3) quantitative coronary analysis (QCA) diameter stenosis greater than 50% with recurrent symptoms or a positive non-invasive test; (4) QCA diameter stenosis greater than 70% by the average of multiple views; or (5) QCA diameter stenosis greater than 70% in the worst view, regardless of other

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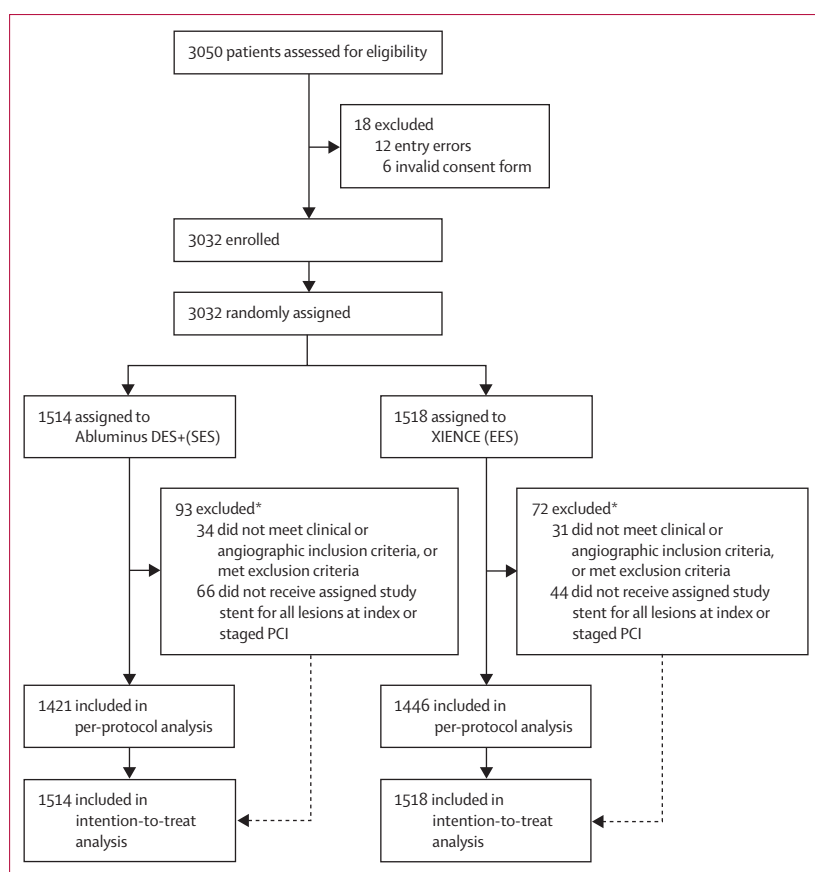


Figure 1: Trial profile

EES=everolimus-eluting stent. PCI=percutaneous coronary intervention. SES=sirolimus-eluting stent. *Reasons for exclusion were not mutually exclusive.

criteria. Myocardial infarction was defined according to the Fourth Universal Definition of Myocardial Infarction;¹⁶ stent thrombosis was classified according to the Academic Research Consortium-2 consensus document.¹⁵ All endpoints reported here were prespecified in the trial protocol and are presented in accordance with the statistical analysis plan; full study endpoint definitions are reported in the appendix (pp 13–19). Harms and adverse events were prospectively collected throughout follow-up, verified against source records, and adjudicated by the independent CEC according to prespecified definitions, with adjudication performed on a rolling basis as events were reported.

Statistical analysis

The two primary hypotheses of the study were non-inferiority of the Abluminus DES+ SES compared with the XIENCE EES for the coprimary endpoints of ischaemia-driven target lesion revascularisation and target lesion failure at 12 months in the per-protocol population. If non-inferiority was met for ischaemia-driven target lesion revascularisation, sequential superiority testing was prespecified in the

intention-to-treat population. The intention-to-treat population included all patients randomly assigned to treatment, irrespective of treatment received. The per-protocol population consisted of all patients randomly assigned and treated exclusively with the assigned stent for all lesions and procedures with no major protocol deviations. For ischaemia-driven target lesion revascularisation, the sample size estimation assumed a 7.5% incidence at 1 year and a 2.8% non-inferiority margin. With an anticipated 8% attrition rate, a total of 3000 patients provided 80% power for non-inferiority with a one-sided type 1 error of 0.025 and 80% power for sequential superiority with a minimum detectable effect size of 0.67. For target lesion failure, on the basis of an expected 9% incidence at 1 year and a 3.0% margin, 2252 patients were sufficient, but 3000 were planned to ensure adequate power for both coprimary endpoints, yielding 89% power for target lesion failure. The 1-year rates of the coprimary endpoints were estimated based on two previous trials investigating the XIENCE EES in patients with diabetes.^{17,18} Given the low event rates previously reported for the experimental device in observational studies,¹⁹ non-inferiority margins for both endpoints were set so that any difference up to the margin would not be considered clinically meaningful. During the study, the final sample size was increased to 3050 to preserve power for the per-protocol analysis, accounting for the observed number of protocol deviations. Non-inferiority was assessed using the Farrington–Manning test. Cumulative incidence was estimated with the Kaplan–Meier method, and hazard ratios (HRs) with 95% CIs were calculated using Cox proportional hazards models. Patients with incomplete follow-up were censored at the time of last contact. All other tests used a two-sided α of 0.05. No interim analyses were prespecified. Landmark analyses were performed at 30 days and 12 months after randomisation, with time zero reset at each landmark and analysing subsequent events only among patients who were alive and free of the endpoint of interest at that landmark timepoint.

Analyses were conducted with Stata version 18.0 and SAS version 9.4 at the Icahn School of Medicine at Mount Sinai (New York, NY, USA), with independent validation of primary endpoint analyses at the London School of Hygiene & Tropical Medicine (London, UK).

Role of the funding source

The funder of the study contributed to the study design and reviewed the data, but had no role in data collection, data analysis, data interpretation, or writing of the report.

Results

Between June 12, 2020, and Sept 9, 2022, 3032 patients were enrolled and randomly assigned to PCI with the Abluminus DES+ SES (n=1514) or the XIENCE EES (n=1518). 2931 (96.7%) of 3032 patients completed

	Abluminus DES+ SES (n=1514)	XIENCE EES (n=1518)
Age, years	68 (60–75)	68 (61–74)
Sex		
Female	462/1514 (30.5%)	417/1518 (27.5%)
Male	1052/1514 (69.5%)	1101/1518 (72.5%)
BMI, kg/m ²	28 (25–32)	29 (26–32)
Region of enrolment		
Europe	1166/1514 (77.0%)	1174/1518 (77.3%)
South America	206/1514 (13.6%)	206/1518 (13.6%)
Asia	142/1514 (9.4%)	138/1518 (9.1%)
Clinical presentation		
Silent ischaemia	277/1508 (18.4%)	293/1513 (19.4%)
Stable angina	680/1508 (45.1%)	695/1513 (45.9%)
Unstable angina	203/1508 (13.5%)	192/1513 (12.7%)
NSTEMI	348/1508 (23.1%)	333/1513 (22.0%)
Medical history		
Current smoker	242/1494 (16.2%)	233/1502 (15.5%)
Hypertension	1246/1509 (82.6%)	1294/1514 (85.5%)
Hypercholesterolemia	999/1509 (66.2%)	1003/1513 (66.3%)
Family history of CAD	393/1500 (26.2%)	418/1506 (27.8%)
Congestive heart failure	152/1507 (10.1%)	132/1514 (8.7%)
LVEF, %	55% (50–60%)	55% (50–60%)
Chronic kidney disease	173/1510 (11.5%)	148/1514 (9.8%)
Liver disease	23/1510 (1.5%)	34/1514 (2.2%)
Peripheral artery disease	137/1510 (9.1%)	132/1514 (8.7%)
Previous stroke	79/1510 (5.2%)	92/1514 (6.1%)
Previous myocardial infarction	315/1510 (20.9%)	317/1512 (21.0%)
Previous PCI	349/1510 (23.1%)	319/1513 (21.1%)
Previous CABG	71/1510 (4.7%)	55/1513 (3.6%)
Atrial fibrillation	177/1510 (11.7%)	164/1513 (10.8%)
Chronic lung disease	114/1509 (7.6%)	115/1512 (7.6%)
High bleeding risk	508/1510 (33.5%)	500/1514 (32.9%)

(Table 1 continues in next column)

	Abluminus DES+ SES (n=1514)	XIENCE EES (n=1518)
(Continued from previous column)		
Diabetes status		
Diabetes type		
Type 1	49/1509 (3.2%)	57/1512 (3.8%)
Type 2	1396/1509 (92.5%)	1397/1512 (92.4%)
Medically treated diabetes treatment	1446/1509 (95.8%)	1463/1515 (96.6%)
Insulin	530/1509 (35.1%)	535/1515 (35.3%)
Sensitisers	1090/1509 (72.2%)	1086/1515 (71.7%)
Secretagogues	371/1509 (24.6%)	367/1515 (24.2%)
GLP-1 or GIP agonists	77/1509 (5.1%)	93/1515 (6.2%)
DPP-4 inhibitors	220/1509 (14.6%)	205/1515 (13.5%)
SGLT2 inhibitors	190/1509 (12.6%)	190/1515 (12.5%)
Baseline laboratory values		
HbA _{1c}	7.6% (6.9–8.8)	7.5% (6.7–8.6)
Serum Creatinine, mg/dL	0.9 (0.8–1.2)	0.9 (0.8–1.2)
eGFR, mL/min per 1.73 m ²	74.0 (60.0–90.0)	75.8 (60.0–90.0)
LDL, mg/dL	85.5 (37.8)	88.2 (37.8)
Antithrombotic therapy at discharge		
Aspirin	1407/1508 (92.9%)	1421/1514 (93.6%)
P2Y ₁₂ inhibitor	1480/1508 (97.8%)	1486/1514 (97.9%)
Clopidogrel	1171/1480 (77.3%)	1197/1486 (78.9%)
Ticagrelor	237/1480 (15.7%)	205/1486 (13.5%)
Prasugrel	72/1480 (4.8%)	84/1486 (5.5%)
Oral anticoagulant	182/1508 (12.0%)	184/1486 (12.1%)

Data are n (%), median (IQR), or mean (SD). CABG=coronary artery bypass grafting. CAD=coronary artery disease. DES=drug eluting stent. DPP-4=dipeptidyl peptidase-4. EES=everolimus-eluting stent. eGFR=estimated glomerular filtration rate. GIP=glucose-dependent insulinotropic polypeptide. GLP-1=glucagon-like peptide-1. HbA_{1c}=glycated haemoglobin. LVEF=left ventricle ejection fraction. NSTEMI=non-ST-elevation myocardial infarction. PCI=percutaneous coronary intervention. SES=sirolimus-eluting stent. SGLT2=sodium-glucose cotransporter-2.

Table 1: Summary of demographic and baseline clinical characteristics

follow-up to death or the end of study at 24 months (figure 1). The median follow-up was 366 days (IQR 366–366) for the 12-month analysis and 726 days (724–728) for the 24-month analysis.

Baseline characteristics were well balanced between the two groups (table 1), as were index procedural characteristics (appendix pp 20–21). Median age was 68.0 years (IQR 60–74). 879 (29.0%) of 3032 patients were female and 2153 (71.0%) were male. Data on race or ethnicity were not collected for this study. Of 3032 patients, 2793 (92.1%) had type 2 diabetes with median HbA_{1c} of 7.6% (IQR 6.8–8.7), 1065 (35.1%) received insulin, and 2176 (71.8%) received sensitisers, mainly metformin. Clinical presentation was non-ST-elevation myocardial infarction in 681 (22.5%) of 3032 patients, and 632 (20.8%) had a previous myocardial infarction. Radial access was used in 2521 (83.1%) of 3032; most procedures treated a single vessel with a mean of 1.7 stents (SD 1.0) implanted. Approximately one third

of cases (983 [32.4%] of 3032) were defined as complex PCI, with an even distribution between groups (appendix pp 20–21). Median stent inflation time was longer with the Abluminus DES+ (45 s, IQR 45–47) than with XIENCE EES (24 s, IQR 14–34), and post-dilatation was performed in 2093 (69.5%) of 3010 procedures across the two groups. Technical success was achieved in 2988 (98.9%) of 3022 patients, with no significant differences between the two groups. Most patients were discharged on dual antiplatelet therapy, predominantly with clopidogrel, with no between-group differences. Information on dual antiplatelet therapy cessation and strategies throughout follow-up is provided in the appendix (p 22).

Of 3032 patients comprising the intention-to-treat population, 165 (5.4%) were excluded from the per-protocol primary analysis for major protocol violations, leaving 2867 (94.6%) patients (1421 in the Abluminus DES+ SES group and 1446 in the XIENCE EES

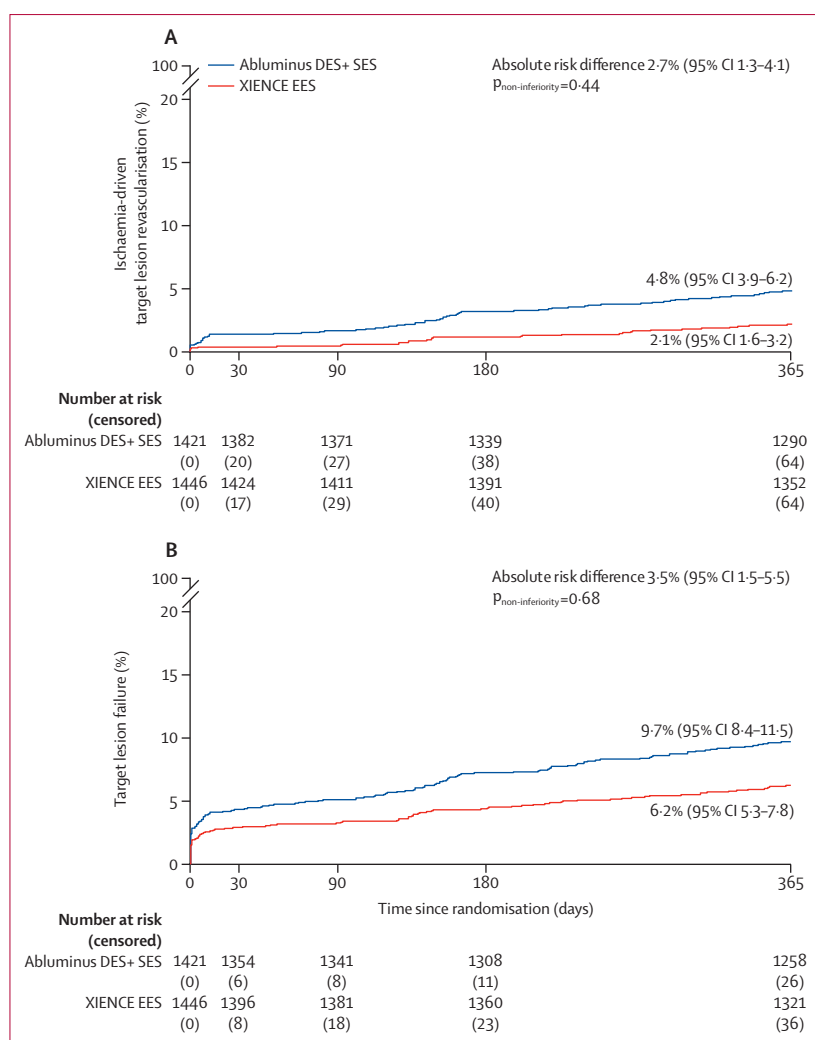


Figure 2: Kaplan-Meier curves for the coprimary efficacy endpoints

Ischaemia-driven target lesion revascularisation (A) and target lesion failure (B) at 12 months in the per-protocol population. DES=drug-eluting stent. EES=everolimus-eluting stent. SES=sirolimus-eluting stent.

group). At 12 months, in the per-protocol population, ischaemia-driven target lesion revascularisation occurred in 67 of 1421 patients (Kaplan-Meier estimate 4.8%, 95% CI 3.9–6.2) in the Abluminus DES+ SES group versus 30 of 1446 patients (2.1%, 1.6–3.2) in the XIENCE EES group (HR 2.31, 95% CI 1.50–3.55), with an absolute risk difference of 2.7% (95% CI 1.3–4.1). The prespecified criterion for non-inferiority was not met ($p_{\text{non-inferiority}}=0.44$), and the lower bound of the 95% CI for the absolute risk difference excluded zero. Similarly, target lesion failure occurred in 137 of 1421 patients (Kaplan-Meier estimate 9.7%, 95% CI 8.4–11.5) in the Abluminus DES+ SES group versus 89 of 1446 (6.2%, 5.3–7.8) in the XIENCE EES group (HR 1.59, 95% CI 1.22–2.07), with an absolute risk difference of 3.5% (95% CI 1.5–5.5). Non-inferiority was not met ($p_{\text{non-inferiority}}=0.68$) and the lower bound of the 95% CI of absolute risk difference excluded zero (figure 2). The

composite of cardiovascular death or target-vessel myocardial infarction was significantly higher in the Abluminus DES+ SES group than the XIENCE EES group (HR 1.55, 95% CI 1.15–2.10), driven by higher rates of target-vessel myocardial infarction (73 of 1421 patients [Kaplan-Meier estimate 5.2%, 95% CI 4.1–6.5] vs 44 of 1446 patients [3.1%, 2.4–4.3]; HR 1.70, 95% CI 1.17–2.47), whereas the difference in cardiovascular death was not statistically significant (41 patients [2.9%, 95% CI 2.1–3.9] vs 30 patients [2.1%, 1.5–3.0]; HR 1.39, 95% CI 0.87–2.23). There were no significant differences in all-cause death or other secondary endpoints (table 2). Analyses at 12 months in the intention-to-treat population were consistent with primary per-protocol results (appendix p 23).

At 24 months, in the intention-to-treat population, ischaemia-driven target lesion revascularisation occurred in 95 of 1514 patients (Kaplan-Meier estimate 6.6%, 95% CI 5.4–7.9) in the Abluminus DES+ SES group versus 57 of 1518 (3.9%, 95% CI 3.0–5.1) in the XIENCE EES group, and target lesion failure in 184 (12.4%, 10.8–14.2) versus 142 (9.6%, 8.2–11.2; table 3, appendix p 27). The composite of cardiovascular death or target-vessel myocardial infarction was higher with the Abluminus DES+ SES. There were no significant differences in all-cause death or cardiovascular death. Definite or probable stent thrombosis occurred in 33 patients (Kaplan-Meier estimate 2.2%, 95% CI 1.6–3.1) and 23 patients (1.6%, 1.0–2.4) in each group, respectively. Other secondary outcomes are reported in table 3. Bleeding events stratified according to high bleeding risk status are reported in the appendix (p 24).

In a landmark analysis from 12 months to 24 months, event rates were low and did not differ between groups for ischaemia-driven target lesion revascularisation and target lesion failure (table 4; appendix p 28). When formally comparing HRs across time intervals, the differences between the 0–12 month HR and the 12–24 month landmark HR were significant for both coprimary endpoints (ischaemia-driven target lesion revascularisation $p=0.039$ and target lesion failure $p=0.016$). An additional 30-day landmark analysis further highlighted the concentration of early events (appendix p 29).

Subgroup analyses at 24 months for the two coprimary endpoints in the intention-to-treat population yielded results consistent with the primary analysis (appendix pp 30–31). Available core-laboratory QCA data for patients with adjudicated ischaemia-driven target lesion revascularisation at 24 months are presented in the appendix (p 25). The most frequent lesion location was in-stent for both groups, whereas edge restenosis was less common in the Abluminus DES+ group. Given the competing risk of death for ischaemia-driven target lesion revascularisation, we also performed a sensitivity analysis using a Fine-Gray subdistribution hazards model (appendix p 26); results were consistent with the primary analysis at both the 12-month and 24-month timepoints.

	Abluminus DES+ SES (n=1421)	XIENCE EES (n=1446)	Hazard ratio (95% CI)	Absolute risk difference, (95% CI)	Non- inferiority margin	P _{non-inferiority}
Target lesion failure	137 (9.7%, 8.4–11.5)	89 (6.2%, 5.3–7.8)	1.59 (1.22–2.07)	3.5% (1.5–5.5)	3.0%	0.68*
Ischaemia-driven target lesion revascularisation	67 (4.8%, 3.9–6.2)	30 (2.1%, 1.6–3.2)	2.31 (1.50–3.55)	2.7% (1.3–4.1)	2.8%	0.44*
Cardiovascular death	41 (2.9%, 2.1–3.9)	30 (2.1%, 1.5–3.0)	1.39 (0.87–2.23)	..	..	..
Target-vessel myocardial infarction	73 (5.2%, 4.1–6.5)	44 (3.1%, 2.4–4.3)	1.70 (1.17–2.47)	..	..	..
Periprocedural	31 (2.2%, 1.5–3.1)	30 (2.1%, 1.5–3.0)	1.05 (0.64–1.74)	..	..	..
Spontaneous	42 (3.0%, 2.3–4.2)	14 (1.0%, 0.7–1.8)	3.09 (1.68–5.65)	..	..	..
Cardiovascular death with target-vessel myocardial infarction	106 (7.5%, 6.2–9.0)	70 (4.9%, 4.0–6.3)	1.55 (1.15–2.10)	..	..	..
All-cause death	52 (3.7%, 2.8–4.8)	48 (3.3%, 2.5–4.4)	1.10 (0.74–1.63)	..	..	..
Definite or probable stent thrombosis	27 (1.9%, 1.3–2.8)	16 (1.1%, 0.7–1.8)	1.73 (0.93–3.21)	..	..	..
Stroke	17 (1.2%, 0.8–2.0)	20 (1.4%, 0.9–2.2)	0.86 (0.45–1.65)	..	..	..
Target-vessel revascularisation (non-target lesion failure)	16 (1.2%, 0.8–2.1)	11 (0.8%, 0.5–1.6)	1.48 (0.69–3.19)	..	..	..
BARC type 2–5 bleeding	50 (3.6%, 2.7–4.7)	51 (3.6%, 2.7–4.7)	1.00 (0.68–1.48)	..	..	..

BARC=Bleeding Academic Research Consortium. DES=drug-eluting stent. EES=everolimus-eluting stent. SES=sirolimus-eluting stent. Non-inferiority was assessed using Farrington–Manning with a one-sided α of 0.025. *Absolute risk differences are shown with two-sided 95% CIs.

Table 2: Primary analysis and secondary outcomes at 12 months in the per-protocol population

Discussion

In this large, international, randomised trial of more than 3000 patients with diabetes undergoing PCI, the Abluminus DES+ SES did not meet the prespecified criteria for non-inferiority compared with the XIENCE EES for the two coprimary endpoints of ischaemia-driven target lesion revascularisation and target lesion failure at 12 months. Observed event rates were lower than anticipated, particularly in the XIENCE EES group, reflecting the good performance of the XIENCE platform. The Abluminus DES+ was associated with higher rates of repeat revascularisation and target-vessel myocardial infarction, and no significant differences between groups in all-cause mortality, cardiovascular mortality, or stent thrombosis were observed. Extended follow-up to 24 months supported these findings, with higher cumulative rates of ischaemia-driven target lesion revascularisation and target-vessel myocardial infarction in the Abluminus DES+ SES group. Landmark analyses indicated that the differences between groups were statistically significant before 1 year, but not thereafter.

The design of the Abluminus DES+ aims to address the biological challenges of diabetes. The device incorporates a biodegradable polymer with sirolimus release, along with a coating on the exposed parts of the delivery balloon. This hybrid approach is intended to augment drug delivery to areas prone to in-stent restenosis, a process that is more aggressive in patients with diabetes.^{3,9} In this trial, the Abluminus DES+ was compared with the XIENCE platform, which is characterised by a durable fluoropolymer and everolimus coating. The comparative efficacy of SES and EES in patients with diabetes has yielded conflicting results. Although some analyses reported similar outcomes between the two antiproliferative drugs,^{20,21}

	Abluminus DES+ SES (n=1514)	XIENCE EES (n=1518)	Hazard ratio (95% CI)
Target lesion failure	184 (12.4%, 10.8–14.2)	142 (9.6%, 8.2–11.2)	1.32 (1.06–1.65)
Ischaemia-driven target lesion revascularisation	95 (6.6%, 5.4–7.9)	57 (3.9%, 3.0–5.1)	1.71 (1.23–2.37)
Cardiovascular death	63 (4.3%, 3.3–5.4)	53 (3.6%, 2.8–4.7)	1.19 (0.83–1.72)
Target-vessel myocardial infarction	87 (5.9%, 4.8–7.2)	57 (3.8%, 3.0–4.9)	1.54 (1.11–2.16)
Periprocedural	34 (2.2%, 1.6–3.1)	32 (2.1%, 1.5–3.0)	1.07 (0.66–1.73)
Spontaneous	53 (3.8%, 2.9–4.9)	25 (1.7%, 1.2–2.5)	2.24 (1.39–3.59)
Cardiovascular death with target- vessel myocardial infarction	139 (9.3%, 8.0–10.9)	105 (7.1%, 5.9–8.5)	1.34 (1.04–1.73)
All-cause death	87 (5.9%, 4.8–7.2)	93 (6.3%, 5.2–7.7)	0.94 (0.70–1.26)
Definite or probable stent thrombosis	33 (2.2%, 1.6–3.1)	23 (1.6%, 1.0–2.4)	1.45 (0.85–2.47)
Stroke	26 (1.8%, 1.2–2.7)	28 (2.0%, 1.4–2.9)	0.93 (0.55–1.59)
Target-vessel revascularisation (non-TLR)	28 (2.0%, 1.3–2.8)	26 (1.8%, 1.2–2.7)	1.08 (0.63–1.84)
Bleeding BARC 2–5	62 (4.2%, 3.3–5.4)	64 (4.4%, 3.4–5.6)	0.98 (0.69–1.38)

BARC=Bleeding Academic Research Consortium. DES=drug-eluting stent. EES=everolimus-eluting stent. SES=sirolimus-eluting stent.

Table 3: Primary and secondary outcomes at 24 months in the intention-to-treat population

others have suggested a potential advantage of everolimus in this population.^{22,23} In patients with diabetes, the exaggerated smooth muscle proliferation and impaired endothelial repair are driven by upregulated PI3K/Akt/mTOR signalling and chronic inflammation.²⁴ Everolimus, with its higher lipophilicity and faster tissue penetration, might better suppress this hyperproliferative milieu and allow earlier endothelial recovery. By contrast, the slower uptake and prolonged retention with sirolimus might be less effective in counteracting the aggressive

	Abluminus DES+ SES (n=1514)	XIENCE EES (n=1518)	Hazard ratio (95% CI)
Target lesion failure			
0–12 months	151 (10.1%, 8.8–11.9)	100 (6.7%, 5.7–8.3)	1.54 (1.19–1.98)
12–24 months	33 (2.6%, 1.7–3.5)	42 (3.2%, 2.2–4.0)	0.81 (0.51–1.28)
Ischaemia-driven target lesion revascularisation			
0–12 months	75 (5.1%, 4.2–6.5)	36 (2.4%, 1.9–3.5)	2.13 (1.43–3.16)
12–24 months	20 (1.5%, 0.9–2.2)	21 (1.5%, 0.9–2.2)	0.98 (0.53–1.81)
Cardiovascular death			
0–12 months	46 (3.1%, 2.3–4.1)	33 (2.2%, 1.6–3.1)	1.40 (0.90–2.19)
12–24 months	17 (1.2%, 0.8–2.0)	20 (1.5%, 0.9–2.3)	0.85 (0.45–1.63)
Target-vessel myocardial infarction			
0–12 months	81 (5.4%, 4.4–6.7)	49 (3.3%, 2.6–4.4)	1.67 (1.17–2.38)
12–24 months	6 (0.5%, 0.2–1.1)	8 (0.6%, 0.2–1.0)	0.77 (0.27–2.22)

DES=drug-eluting stent. EES=everolimus-eluting stent.

Table 4: Landmark analysis of coprimary endpoints and its components at 0–12 months and 12–24 months in the intention-to-treat population

neointimal response of diabetes.²⁵ Nonetheless, large-scale studies seem to indicate that diabetes primarily increases the risk for repeat revascularisation consistently across the spectrum of coronary artery disease complexity and irrespective of the stent platform.¹¹

Placed in the context of previous studies, the performance of the XIENCE group in this study exceeded its historical data.²⁶ Indeed, the XIENCE platform had shown good outcomes in patients with diabetes, with 2-year target lesion failure rates of 10.1% and target lesion revascularisation rates of 5.5% in a pooled analysis of SPIRIT II-IV and COMPARE trials.¹⁰ Event rates were even lower in the TUXEDO trial, in which the paclitaxel-eluting stent, Taxus, did not meet non-inferiority²⁷ and the primary endpoint of target-vessel failure occurred in only 4.3% of patients treated with XIENCE stents at 2 years.²⁷ Recently, a small mechanistic study randomly assigned 131 patients with diabetes to Abluminus DES+ or XIENCE stents and used optical coherence tomography-derived neointimal volume at 9–12 months as the primary endpoint.¹⁴ The trial did not show an advantage of the Abluminus DES+, as there were no significant differences in neointimal volume, neointimal obstruction, or clinical outcomes between the two devices. In our study, the Abluminus DES+ did not provide further improvements beyond the benchmark set by the XIENCE platform, although its performance aligned with other contemporary stents tested in patients with diabetes. In the SUGAR trial (n=1175),²⁸ the polymer-free amphilimus (sirolimus plus fatty acid) eluting stent Cre8 EVO was non-inferior and superior to the durable-polymer zotarolimus-eluting Resolute Onyx stent with respect to 1-year target lesion failure (7.2% vs 10.9%, respectively). However, at 2 years, differences between the stents were no longer statistically significant, with pooled target lesion failure and target lesion revascularisation rates of approximately 11% and 7%,

respectively.²⁹ Conversely, in our study, landmark analyses from 12 months to 24 months showed parallel event curves, indicating that the excess risk with the Abluminus DES+ was confined to the first year and outcomes thereafter were similar, excluding a persistent hazard. Of note, the SUGAR trial had a higher proportion of patients with acute coronary syndrome and included patients with non-ST-elevation myocardial infarction, which might have affected event rates. However, the late catch-up observed beyond 1 year is less likely related to clinical presentation. By contrast, although this study was characterised by longer total stent length and a higher frequency of left-main and staged PCI—factors associated with complexity and ischaemic risk—the study population was predominantly stable.

Several additional factors might help to contextualise the findings of the present study. Nearly three-quarters of participating sites were new to the Abluminus DES+, and more than 10% of patients did not receive implantation according to the instructions for use. The procedural requirement for prolonged balloon inflation (>45 s) to ensure uniform drug deposition might also have added technical difficulties, particularly in multivessel or complex lesions. To better clarify whether site volume and presence of a learning curve could have affected outcome, we performed multiple sensitivity analyses according to site volume and by excluding early cases. These analyses did not identify meaningful differences from the primary results (data not shown). However, because the analyses were conducted at the site level, and operator-level data were not available, some degree of operator-specific experience cannot be fully excluded as a contributing factor. Additionally, this study found a higher incidence of target-vessel myocardial infarction with the Abluminus DES+, primarily driven by spontaneous rather than periprocedural events. The absence of a difference in periprocedural myocardial infarction is reassuring, given the implantation technique of the Abluminus DES+, which requires longer balloon inflation times. Conversely, the increased rate of spontaneous myocardial infarction diverges from previous observational studies with the Abluminus DES+, which reported lower event rates, and warrants further investigation.^{30,31} Mechanistically, potential explanations for the excess of spontaneous target-vessel myocardial infarction might relate to device-specific characteristics. The elution kinetics of the Abluminus DES+ are designed to provide an initial burst release in the first 7 days, followed by sustained release for more than 90 days. Although transient local inflammation or prothrombotic activity during polymer degradation cannot be excluded, preclinical studies of the Abluminus DES+ have shown complete early endothelialisation and no evidence of increased inflammation.³² By contrast, the durable fluoropolymer coating of XIENCE provides stable drug release and has fluoropassivation properties associated with low thrombogenicity and enhanced endothelial

healing.^{33–35} Given the high adherence to dual antiplatelet therapy, with similar antiplatelet type, duration, and cessation patterns across both groups, differences in exposure to antiplatelet therapy are unlikely to have contributed meaningfully to the divergent outcomes observed. The observed imbalance in spontaneous target-vessel myocardial infarction should be interpreted with caution, given that the absolute risk difference was 2.1% and that the trial was not powered for individual ischaemic endpoints. Therefore, a chance finding rather than a true device-related effect cannot be excluded.

Beyond device-specific considerations, the results of this study provide broader insights about PCI in patients with diabetes, who remain at high risk of adverse outcomes even with the newest DES platforms, with rates of target lesion failure exceeding 9% at 2 years. The FREEDOM trial⁵ showed that CABG was superior to PCI for patients with diabetes and multivessel disease; yet, many of these patients remain at high risk of poor outcomes from surgery due to anatomical or clinical considerations, in addition to patient preference. Continuous innovation in DES design, optimisation of antithrombotic therapy, and adjunctive strategies to address diffuse atherosclerosis remain essential. In this context, this trial underscores the ongoing unmet need to reduce residual ischaemic risk in patients with diabetes. New technologies, such as drug-coated balloons, might provide an alternative strategy for selected lesions by avoiding stent implantation, potentially reducing the burden of neointimal proliferation and late adverse events.³⁶

This study has limitations. First, operator awareness of study device assignment might have introduced bias. However, the clinical team performing follow-up remained masked, as did the independent clinical events committee responsible for endpoint adjudication. Second, the use of intravascular imaging was not systematically collected. Given that imaging use was left to operator discretion, we cannot exclude a potential influence of differential imaging guidance on outcomes, although such use was likely balanced by randomisation. Third, although the study was adequately powered for the prespecified non-inferiority analyses, event rates at 12 months were lower than expected. Fourth, the trial was not powered for mortality or other individual ischaemic endpoints. Finally, follow-up was limited to 24 months, and longer observation might be needed to ascertain whether event rates remain stable over time.

In summary, to our knowledge, ABILITY Diabetes Global is the largest randomised trial to date comparing two contemporary DES platforms in patients with diabetes undergoing PCI. The findings underscore the persistent residual risk in patients with diabetes and highlight the ongoing need for innovation in stent technology, procedural optimisation, and adjunctive pharmacotherapies to further reduce the risk of ischaemic events in this population.

Contributors

RM and M-CM conceived and designed the study, with input from AA, AC, and SSai. M-CM and RM were responsible for trial management, execution, and site coordination. AA, DCh, RS, FM, MV, AK, PC, BF, PG, DH-S, AI, NL, SK, DM, KM, VP, TS, KT, LT, RT, FV, JW, and AC contributed to data collection and patient recruitment. Statistical analyses were performed by SSai, with oversight from AO, DCa, and BV. AA, DCa, BV, and AO accessed and verified the data underlying the manuscript. AA, AO, M-CM, and RM drafted the manuscript, with critical input and revisions from all authors. All authors had access to the all the included data and vouch for the accuracy of the data and the fidelity of the trial to the protocol. All authors reviewed and approved the final version of the report and take responsibility for its accuracy and integrity. The decision to submit the manuscript for publication was made collectively by all authors.

Declaration of interests

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Data sharing

Patient-level data collected for this study will not be made publicly available. However, de-identified participant data underlying the results reported in this Article, together with the study protocol, statistical analysis plan, and data dictionary, can be made available on reasonable request to the corresponding author and with approval of the study sponsor. Data can be made available from with publication of this Article and for 5 years thereafter. Access will be granted following submission and approval of a methodologically sound research proposal and the signing of a data access agreement. Statistical code used for the analyses will also be available upon request under the same conditions.

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