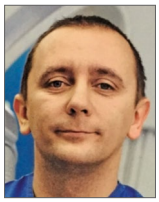
Neointimal hyperplasia of ultra-thin stents with microcrystalline sirolimus or durable polymer everolimus-eluting stents: 6- and 24-month results of the DESSOLVE III OCT study



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KEYWORDS

- drug-eluting stent
- optical coherence tomography
- quantitative coronary angiography

Abstract

Aims: The DESSOLVE III OCT substudy aimed to compare serially neointimal hyperplasia volume obstruction (%VO) between the thin-strut MiStent with early polymer elimination and nine-month sustained drug release from microcrystalline sirolimus and the durable polymer-coated everolimus-eluting XIENCE stent at six and 24 months after implantation.

Methods and results: The efficacy endpoint was %VO, calculated as abluminal neointimal volume/stent volume. Thirty-six patients (MiStent 16 patients, 16 lesions; XIENCE 20 patients, 22 lesions) underwent serial OCT evaluation at both six and 24 months. At six months, mean abluminal %VO was significantly lower in the MiStent group than in the XIENCE group (14.54±3.70% vs 19.11±6.70%; p=0.011), whereas the difference in %VO between the two groups decreased at 24 months (20.88±5.72% vs 23.50±7.33%; p=0.24). There was no significant difference in percentage malapposed struts and percentage uncovered struts between the two groups at both time points.

Conclusions: In the serial comparative OCT analysis of the MiStent versus the XIENCE, the MiStent showed a more favourable efficacy for preventing neointimal formation with comparable strut tissue coverage, as compared with the XIENCE at six months, but this difference in %VO decreased at 24 months so that the difference in neointima at 24 months was no longer significant.

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Abbreviations

DES drug-eluting stent
MLD minimum lumen diameter
OCT optical coherence tomography
PCI percutaneous coronary intervention
QCA quantitative coronary angiography

Introduction

Conventional drug-eluting stents (DES) combine short-term drug release (<90 days) with the permanent presence of a polymer on the stent surface, which could contribute to late progression of neointimal thickness, hypersensitivity reactions and neoatherosclerosis formation with a subsequent increased risk for stent thrombosis, acute myocardial infarction, sudden death and revascularisation at long-term follow-up[1,2]. In contrast, a slow release of drug with prolonged retention in the tissue and early elimination of the polymer coating has the potential to reduce neointimal proliferation and a risk of both early and late stent failure[3-6].

The aim of the DESSOLVE III OCT substudy was to analyse abluminal in-stent neointimal hyperplasia volume obstruction (%VO) – a histomorphometric surrogate of neointima – at six and 24 months after implantation of a three-month absorbable polymer-coated, thin-strut coronary stent system using a crystalline form of sirolimus (MiStent®; Micell Technologies, Durham, NC, USA). Here, we present the serial comparison of optical coherence tomography (OCT) imaging results between the MiStent and the commercially available durable polymer-coated everolimus-eluting XIENCE stent (Abbott Vascular, Santa Clara, CA, USA).

Methods

STUDY DESIGN

The DESSOLVE III OCT study is a substudy of the DESSOLVE III randomised controlled trial (RCT), which was designed to compare the MiStent with the XIENCE stent in an all-comers population (n=1,398)[7-9]. The current OCT substudy was performed at three interventional cardiology centres in Poland. Patients for the OCT substudy consented to undergo six- and 24-month follow-up with repeat catheterisation and OCT imaging. Participants had to meet the inclusion criteria of the DESSOLVE III main study (NCT02385279) and specific criteria related to the OCT substudy. The main inclusion criterion was one single *de novo* lesion in a native coronary artery with stenosis of ≥50% successfully treated with the study stents. The main exclusion criteria for the OCT substudy included bifurcation lesions, total occlusions, left main lesions, lesions with overlapping stents, severely tortuous lesions, calcified or angulated anatomy of the study vessel that, in the opinion of the investigator, could result in suboptimal imaging or excessive risk of complication from placement of an OCT catheter.

OCT imaging was performed with the use of an OCT system (ILUMIEN™ imaging system) and Dragonfly™ catheters (both Abbott Vascular) using a non-occlusive technique with intracoronary injection of contrast agent and following standard techniques recommended by the manufacturer.

The study was performed in accordance with the Declaration of Helsinki and Good Clinical Practices after approval of the local ethics committee.

DEVICE DESCRIPTION

The detailed design of the MiStent has been described elsewhere[10]. Briefly, the MiStent is a thin-strut (64 µm) cobalt-chromium stent coated with biodegradable polylactide-co-glycolic acid (PLGA) that contains a crystalline form of sirolimus. The PLGA begins to flow off the stent in 45-60 days and is fully absorbed within 90 days, embedding microcrystals of sirolimus in the vessel wall with a therapeutic drug presence of up to nine months[4]. The XIENCE V® cobalt-chromium stent (Abbott Vascular) is covered with a durable fluoropolymer that releases 80% of everolimus within the first 30 days after deployment[11] **(Figure 1)**.

OCT AND QUANTITATIVE CORONARY ANGIOGRAPHY (QCA) ANALYSIS

There are two types of measurement of neointimal hyperplasia post stenting. One considers the endoluminal optical leading edge of the strut and connects by interpolation of these leading edges to form a circular boundary (endoluminal stent contour). This circular boundary and the luminal contour comprise the circumferential neointima covering the struts. The second assessment (abluminal stent contour) takes into account the virtual abluminal backside of the struts – that vary in thickness as a function of the stent design (64 ≈ 65 µm for MiStent; 81+7.8 ≈ 90 µm for XIENCE) – to delineate automatically the abluminal backside of the struts **(Supplementary Figure 1)**[12]. On OCT, the abluminal stent contour can indicate the original lumen border and allow quantification of neointimal hyperplasia[12]. Quantitative OCT assessment was performed at every 1.0 mm interval using QIvus software, version 3.0 (Medis, Leiden, the Netherlands).

In QCA analyses, the stented segment and the peri-stent segments (defined by a length of 5 mm proximal and distal to the stent edge), as well as their combination (in-segment analysis), were analysed[13]. Late loss was defined as the difference in minimum lumen diameter (MLD) between post procedure and follow-up. QCA assessment was performed using the Coronary Angiography Analysis System, version 5.11 (Pie Medical Imaging, Maastricht, the Netherlands).

Both analyses were performed by an independent core laboratory (Cardialysis B.V., Rotterdam, the Netherlands) and the analysts were blinded to the device type.

OCT ENDPOINTS AND DEFINITIONS

The primary endpoint was the pre-specified six-month abluminal in-stent %VO, calculated as the mean abluminal neointimal volume/mean abluminal stent volume ×100. Quantitative OCT assessment on the following endpoints was also performed: (1) mean and minimal lumen area, (2) mean and minimal stent area, (3) stent symmetry, (4) stent expansion, (5) mean neointimal hyperplasia area, (6) percentage of malapposed struts, (7) percentage of covered and uncovered struts, and (8) neointimal healing

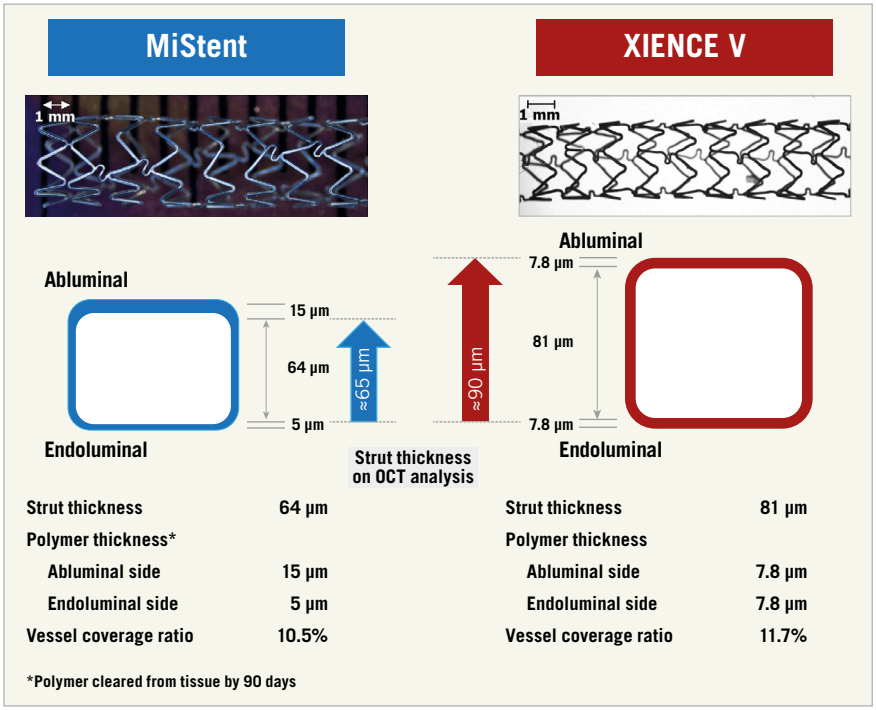

Figure 1. *Strut thickness calculation on the follow-up OCT analysis. At six months, the asymmetric bioresorbable polymer has disappeared so that the true thickness of the MiStent is approximately 65 µm, whereas with the XIENCE the symmetric durable coating will persist so that the thickness of a combination of metallic struts and coating is approximately 90 µm (81+7.8 ≈ 90). These two values of strut thickness were used in the abluminal OCT assessment. The endoluminal polymer thickness should be negligible for assessment due to the blooming of the metallic strut on OCT.*

score. The calculation method of the healing score is presented in **Supplementary Appendix 1** [14].

STATISTICAL ANALYSIS

The details of the statistical analysis are presented in **Supplementary Appendix 2**.

Results

STUDY SUBJECTS

Twenty-five (25) patients (25 lesions) in the MiStent group and 28 patients (30 lesions) in the XIENCE group underwent repeat catheterisation with QCA and OCT assessment at six-month follow-up. Subsequently, 16 patients (17 lesions) in the MiStent group and 21 patients (23 lesions) in the XIENCE group underwent QCA and OCT at 24 months. Serial evaluation was available in 16 patients (16 lesions) in the MiStent group and 20 patients (22 lesions) in the XIENCE group due to the refusal of nine patients, three adverse events between six and 24 months (one death in the MiStent group; one death and one target lesion revascularisation [TLR] in the XIENCE group), and two non-analysable cases **(Figure 2)**.

BASELINE CHARACTERISTICS AND PROCEDURAL DATA

There was no significant difference in baseline clinical characteristics and procedural data except for the mean maximum pressure used for predilatation between the MiStent and the XIENCE group **(Table 1)**. There were no significant differences in coronary lesion distribution between the two stents.

Preprocedural QCA parameters were also comparable between the two groups. However, lesions in the MiStent group were better and more aggressively prepared in terms of balloon predilatation. These lesions were numerically more often predilated, and significantly higher predilatation pressures were applied in this group (p=0.03). However, the maximal size of the expected balloon diameter according to the charts provided by the manufacturers was not significantly different between the two groups (p=0.53). Two and five lesions were post-dilated in the MiStent and XIENCE group, respectively. In post-procedural QCA, in-stent MLD was comparable between the two groups (p=0.25).

OCT RESULTS

Abluminal quantitative OCT results are presented in **Table 2**. The endoluminal OCT results are presented in **Supplementary Table 1**. The mean stent area was comparable between the two stents at both six and 24 months. Compared with the XIENCE, the mean %VO was significantly lower in the MiStent group at six months (14.54±3.70 vs 19.11±6.70; p=0.011), whereas this difference decreased at 24 months (20.88±5.72 vs 23.50±7.33; p=0.24). The late neointimal hyperplasia of the MiStent between six and 24 months was comparable to that of the XIENCE (6.35±4.17 vs 4.39±4.59; p=0.19).

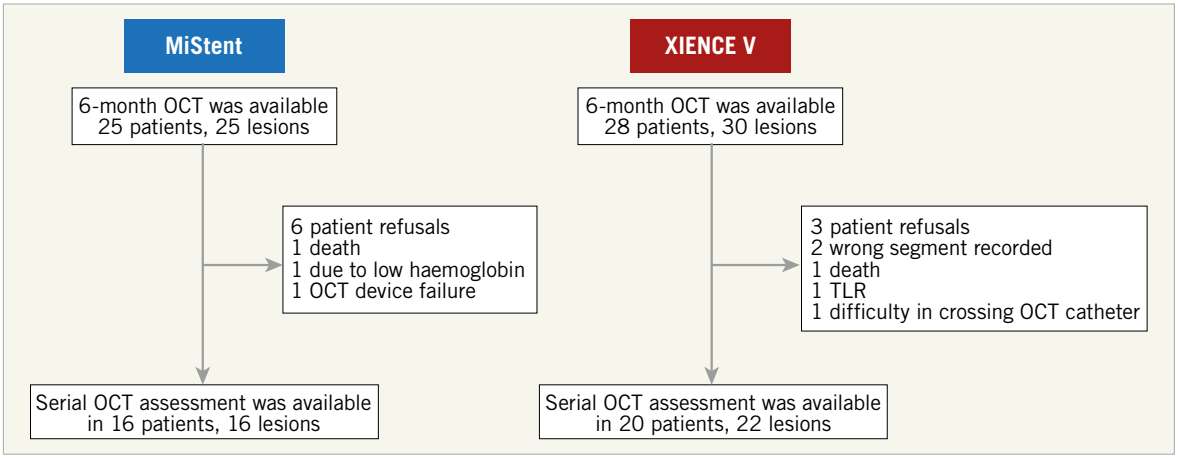

Figure 2. *Flow diagram of participants in the DESSOLVE III OCT substudy.*

Minimum lumen area was comparable between the two stents at six months (p=0.63) and 24 months (p=0.99). The MiStent was comparable to the XIENCE in terms of mean lumen area at six months (p=0.94) and 24 months (p=0.81).

In both study groups, there was only a minimal number of malapposed struts (MiStent: 1.7±3.4 vs XIENCE: 0.6±1.0; p=0.23, at six months; 0.7±1.9 vs 0.4±1.0; p=0.51, at 24 months) and practically all analysed struts were completely covered at both time points. There was also no significant difference in abluminal healing score between the two groups at six and 24 months.

Representative cases of the MiStent and the XIENCE are shown in **Figure 3**.

Table 1. Baseline characteristics and procedural data.

	MiStent (16 patients, 16 lesions)	XIENCE (20 patients, 22 lesions)	*p*-value
Baseline clinical characteristics			
Male	9 (56.3)	14 (70)	0.39
Age (years)	66.5±8.4	65.2±9.1	0.66
Diabetes mellitus	2 (12.5)	6 (30)	0.21
Hypertension	12 (75)	19 (95)	0.08
Dyslipidaemia	12 (75)	14 (70)	0.95
Renal failure	1 (6.3)	0 (0)	0.27
Previous myocardial infarction	4 (25)	4 (20)	0.72
Previous percutaneous coronary intervention	9 (56.3)	6 (30)	0.11
Previous coronary artery bypass grafting	1 (6.3)	1 (5.0)	0.87
Chronic obstructive pulmonary disease	1 (6.3)	1 (5.0)	0.87
Procedural data			
Left anterior descending artery	6 (37.5)	12 (54.5)	0.30
Left circumflex artery	5 (31.3)	3 (13.6)	0.19
Right coronary artery	5 (31.3)	7 (31.8)	0.97
Left main	0 (0)	0 (0)	NA
Nominal stent diameter (mm)	2.86±0.31	2.88±0.32	0.92
Total nominal stent length (mm)	22.5±13.65	22.14±8.13	0.92
Direct stenting	7 (43.8)	16 (72.7)	0.07
Predilatation	9 (56.3)	6 (27.3)	0.07
Mean maximum pressure used for predilatation (atm)	13.89±2.76	10.67±2.07	0.03
Maximal balloon size used for predilatation (based on actual pressure) to nominal stent size	0.78±0.08	0.75±0.13	0.53
Post-dilation	2 (12.5)	5 (22.7)	0.42
Mean maximum pressure used for post-dilatation (atm)	16.5±0.71	19.8±5.67	0.47

Data are expressed as mean±SD and n (%).

Table 2. Abluminal quantitative OCT results at 6 and 24 months.

	6 months				24 months			
	MiStent (16 patients, 16 lesions)	XIENCE (20 patients, 22 lesions)	Difference [95% CI]	*p*-value	MiStent (16 patients, 16 lesions)	XIENCE (20 patients, 22 lesions)	Difference [95% CI]	*p*-value
Length of stented region (mm)	19.18±6.15	23.28±7.88	–4.10 [–8.91, 0.70]	0.09	19.20±5.95	22.28±7.55	–3.08 [–7.70, 1.54]	0.18
Mean lumen area (mm^2)	5.87±1.40	5.83±1.81	0.04 [–1.06, 1.14]	0.94	5.41±1.29	5.55±1.91	–0.13 [–1.25, 0.99]	0.81
Minimal lumen area (mm^2)	4.57±1.07	4.35±1.56	0.22 [–0.70, 1.14]	0.63	4.03±0.92	4.03±1.71	–0.0 [–0.96, 0.95]	0.99
Mean stent area (mm^2)	6.65±1.60	7.00±1.84	–0.35 [–1.51, 0.81]	0.54	6.73±1.55	7.06±1.95	–0.33 [–1.53, 0.87]	0.58
Minimal stent area (mm^2)	5.53±1.27	5.77±1.62	–0.24 [–1.23, 0.75]	0.63	5.46±1.22	5.82±1.77	–0.36 [–1.40, 0.69]	0.49
Mean neointimal hyperplasia area (mm^2)	0.96±0.32	1.29±0.43	–0.33 [–0.59, –0.06]	0.016	1.42±0.52	1.58±0.36	–0.16 [–0.45, 0.13]	0.27
Neointimal hyperplasia volume obstruction (%)	14.54±3.70	19.11±6.70	–4.57 [–8.34, –0.81]	0.011	20.88±5.72	23.50±7.33	–2.62 [–7.09, 1.85]	0.24
Minimum stent eccentricity	0.80±0.08	0.85±0.05	–0.05 [–0.09, –0.00]	0.06	0.79±0.08	0.83±0.05	–0.05 [–0.09, –0.00]	0.038
Stent asymmetry index	0.26±0.08	0.24±0.07	0.02 [–0.03, 0.07]	0.38	0.29±0.08	0.25±0.08	0.04 [–0.01, 0.09]	0.15
Stent expansion	0.92±0.22 (15)	1.13±0.25 (21)	–0.21 [–0.37, –0.04]	0.016	1.00±0.29 (15)	1.24±0.44 (21)	–0.23 [–0.50, 0.03]	0.08
Healing score	1.71±3.42	0.66±1.28	1.05 [–0.56, 2.66]	0.19	3.86±6.12	2.93±5.29	0.93 [–2.84, 4.69]	0.62
Modified healing score	1.71±3.42	1.1±1.75	0.6 [–1.12, 2.32]	0.48	4.03±6.04	3.99±5.58	0.04 [–3.81, 3.89]	0.98
Total number of struts	190.9±63.9	229.2±71.7	–38.3 [–84.0, 7.4]	0.10	197.4±64.0	227.4±70.1	–29.9 [–75.0, 15.1]	0.19
Percentage covered struts (%)	99.9±0.3	100.0±0.1	–0.1 [–0.3, 0.0]	0.14	98.4±2.9	98.7±2.3	–0.3 [–2.0, 1.4]	0.69
Percentage uncovered struts (%)	0.1±0.3	0.0±0.1	0.1 [–0.0, 0.3]	0.14	1.6±2.9	1.3±2.3	0.3 [–1.4, 2.0]	0.69
Percentage malapposed struts (%)	1.7±3.4	0.6±1.0	1.1 [–0.4, 2.7]	0.23	0.7±1.9	0.4±1.0	0.4 [–0.6, 1.3]	0.51
Data are presented as mean±SD.								

QCA ANALYSIS

Serial QCA was available in 16 patients and 16 lesions in the MiStent group and in 20 patients and 22 lesions in the XIENCE group. The MLD was numerically higher in the MiStent group than in the XIENCE group at six months (MiStent: 2.28±0.24 mm, XIENCE: 2.07±0.36 mm; p=0.07) and 24 months (2.06±0.27 mm vs 1.97±0.40 mm; p=0.45). Angiographic late loss was numerically lower in the MiStent group than in the XIENCE group at six months (0.02±0.31 mm vs 0.18±0.24 mm; p=0.10); however, this difference was not observed at 24 months (0.26±0.32 mm vs 0.23±0.32 mm; p=0.76). No binary restenosis was observed in either group **(Supplementary Table 2)**.

Discussion

The main findings of the current study can be summarised as follows.

i) Abluminal %VO (efficacy endpoint), so-called histomorphometric neointima, was significantly lower in the MiStent than in the XIENCE at six months. This difference was partially maintained at 24 months.

ii) Strut coverage and malapposition (safety endpoint) were comparable between the two groups at both time points.

iii) The minimal and mean lumen area were comparable between the two groups at six and 24 months.

NEOINTIMAL GROWTH UP TO SIX MONTHS

The current serial OCT analysis, in the context of a randomised trial, demonstrated that the MiStent resulted in a significantly better suppression of neointimal hyperplasia than the XIENCE at six-month follow-up. One potential explanation of this result in favour of the MiStent may reside in the stent expansion index, which was significantly higher in the XIENCE group than in the MiStent group. A higher stent expansion index may affect the amount of neointimal formation by creating larger injury[15]; however, this effect should be counterbalanced by the antiproliferative drug. Furthermore, due to the absence of baseline OCT, it is not possible to assess the impact of embedment of struts on the subsequent neointimal hyperplasia.

The favourable results of the MiStent might also be attributed to the early elimination of the polymer coating (three months) in conjunction with sustained drug release from the sirolimus microcrystals embedded in the vessel wall (nine months) **(Supplementary Figure 2)**. Additionally, the thin stent platform of the MiStent could have played a role in the favourable findings of this study. The importance of prolonged drug delivery was originally demonstrated in the PISCES trial in which paclitaxel, a hydrophilic drug, was effective only if its release kinetics were prolonged for at least 10 or 30 days (as opposed to the shorter time points)[16]. In addition, that study showed that an increase in the drug dose did not play an important role in efficacy, as its concentration may easily exceed receptor capacity, leading to toxic levels with subsequent adverse clinical events[17]. Thus, prolonged delivery of the optimal drug dose adjusted to the binding capacity of the tissues is of paramount importance in the efficacy of tested drug and stent technologies. Furthermore, low levels of drug release with prolonged retention of a drug in the tissue minimise toxic levels, thereby improving the safety of a device[16].

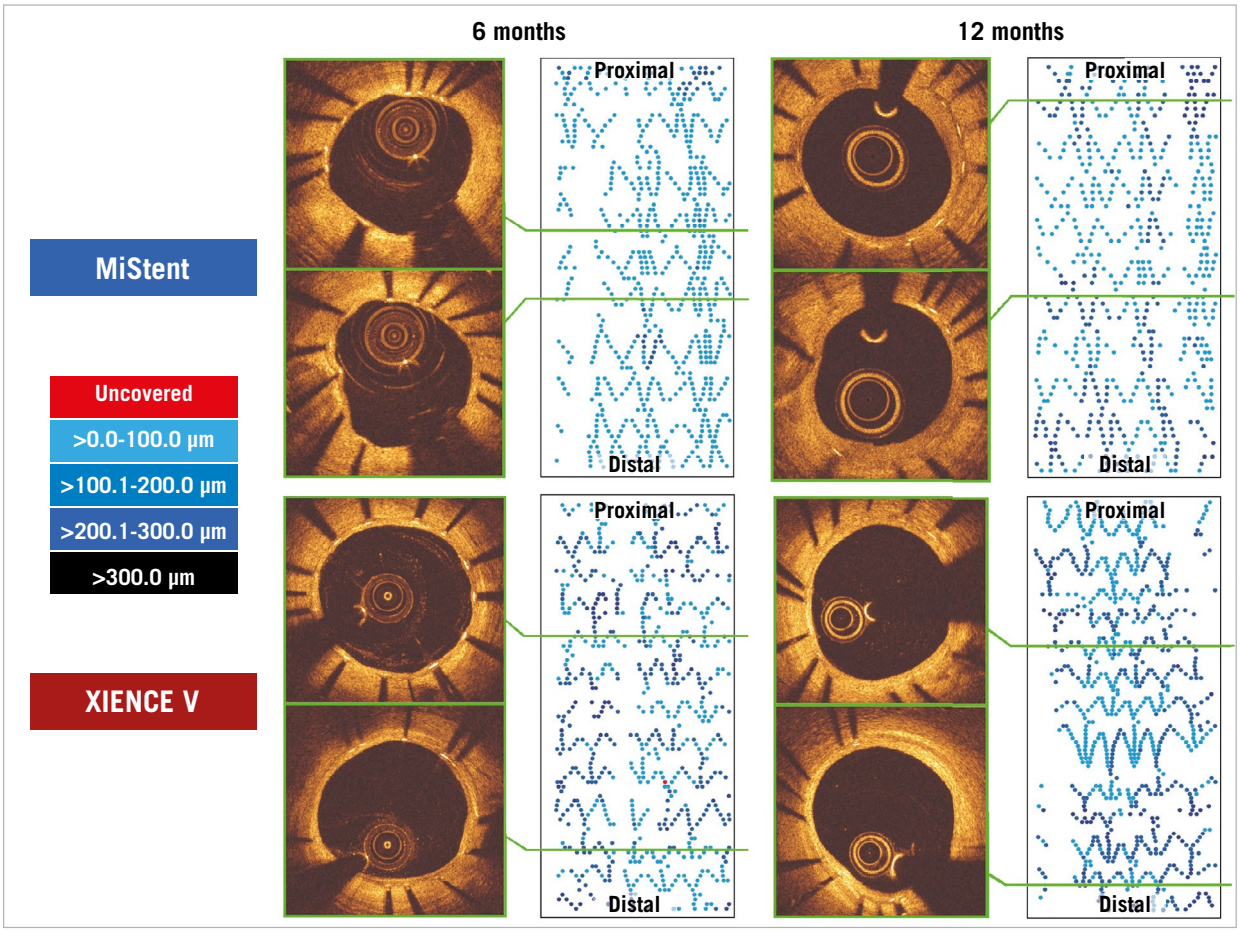

Figure 3. *Representative cases in the DESSOLVE III OCT study involving the MiStent (upper) and the XIENCE stent (lower). Cross-sectional images and 2D fold-out views of strut coverage with colour coding of the neointimal thickness on struts.*

Currently, technological advances allow optimal stent design with controlled and predictable systems of drug elution, avoiding an uncontrolled initial burst. In contrast to the amorphous or aqueous forms of drugs used in previous-generation DES, the currently available crystalline forms of antiproliferative compounds (such as crystalline sirolimus on the MiStent) can provide additional control over drug elution for an extended period of time. The drug locked in crystalline form does not diffuse within the coating after implantation and allows a more desirable drug elution pattern[18]. This system of antiproliferative drug delivery assures not only long-term antiproliferative effects, but, in the case of sirolimus with its anti-inflammatory properties, may also minimise potential inflammatory reactions caused by polymers[19].

NEOINTIMAL GROWTH BETWEEN SIX AND 24 MONTHS

In the current OCT substudy, the significant inhibition of %VO at six months in the MiStent group was no longer observed at 24 months; the delta %VO between six and 24 months was also not significantly different between the two stents. Although we expected that the potential benefit of prolonged drug release in the absence of polymer would result in less neointimal proliferation, the expected effect was not observed in this series. Late neointimal growth has also been observed in other DES types including the XIENCE stent[20]. The mechanisms for this phenomenon are still unclear. The longer duration of drug elution even at a low level might be associated with a delayed late catch-up of neointimal hyperplasia of the MiStent once the upregulation of p27 is eliminated[21]. Late neointimal growth might be an adaptive biological reaction of the vessel, aimed at homogenising shear stress towards physiological values[22]. Alternatively, that might be related to a delayed healing response of the vessel or to a hypersensitivity reaction to durable polymers[23].

The current serial OCT analysis found that the MiStent group had low %VO of 14.50 and 20.88 on OCT at six and 24 months, respectively, which was corroborated with the late loss and in-segment diameter stenosis on QCA at six and 24 months. Asano et al reported that angiographic late loss (usually driven by neointimal growth) below the threshold of 0.50 mm was not associated with an increased risk for TLR and may be considered as a subclinical level of neointimal hyperplasia. Beyond the threshold value of 0.50 mm, there was an exponential increase in TLR[24]. In the current serial QCA assessment, the MiStent had late loss of 0.02 and 0.26 mm and in-segment percent diameter stenosis of 15.1% and 18.4% on QCA at six and 24 months, respectively.

These values of late loss and in-segment percent diameter stenosis corresponded with those of new DES approved by the Food and Drug Administration according to a report of the European Society of Cardiology and the European Association of Percutaneous Cardiovascular Interventions Task Force[25]. In the DESSOLVE III main study, the rate of clinically indicated TLR was comparable between the two groups at 24 months (MiStent 4.6% vs XIENCE 5.4%, difference -0.9% [95% CI: −3.2 to 1.4], p=0.447).

Limitations

The current OCT analysis should be interpreted in the context of the following limitations. First, although the current study is a substudy of the DESSOLVE III RCT, the randomisation was not implemented for the two device groups. Second, this study included a small number of patients without formal sample size calculation. Therefore, the results are regarded as exploratory. Third, the current OCT results were reported using the abluminal stent contour. The abluminal contour could indicate the original lumen border on the assumption that all struts are apposed. Thus, in case of embedded or buried struts at baseline, we might have overestimated neointimal growth in the XIENCE group, since the XIENCE has a thicker strut thickness than the MiStent.

Conclusions

In the serial comparative OCT analysis of the MiStent versus the XIENCE stent, the MiStent showed a more favourable efficacy for preventing neointimal formation with comparable strut tissue coverage, as compared with the XIENCE stent at six months. However, this difference in %VO decreased at 24 months so that the difference in neointima at 24 months was no longer significant.

Impact on daily practice

The current serial OCT assessment demonstrated that the MiStent with early polymer elimination and nine-month sustained drug release had not only a more potent efficacy of neointimal inhibition but also a comparable strut coverage at six months, compared with the XIENCE stent and that this intergroup difference was partially maintained at 24 months. Although the study was not powered to detect differences in clinical outcomes, the MiStent may become an option as a contemporary drug-eluting stent with a potentially low revascularisation rate in short-term follow-up and a similar safety profile to the XIENCE stent.

Guest Editor

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Conflict of interest statement

W. Wijns reports grants from Micell during the conduct of the study, grants from MicroPort, personal fees from Biotronik and Abbott Vascular, outside the submitted work, and being a co-founder of Argonauts, an innovation facilitator. P.W. Serruys reports personal fees from Abbott Laboratories, AstraZeneca, Biotronik, Cardialysis, GLG Research, Medtronic, Sino Medical Sciences Technology, Société Europa Digital & Publishing, Stentys France, Svelte Medical Systems, Philips/Volcano, St. Jude Medical, Qualimed, and Xeltis, outside the submitted work. The Guest Editor is a consultant for Edwards Lifesciences. The other authors have no conflicts of interest to declare.

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Supplementary data

Supplementary Appendix 1. The calculation method of the (modified) healing score on OCT assessment.

Supplementary Appendix 2. Statistical analysis.

Supplementary Figure 1. Endoluminal and abluminal assessment on OCT that automatically delineates either the endoluminal leading edge of the strut or the abluminal backside of the strut.

Supplementary Figure 2. Time course for drug delivery and polymer degradation in various drug-eluting stents with bioresorbable coating.

Supplementary Table 1. Endoluminal quantitative OCT results at 6 and 24 months.

Supplementary Table 2. Baseline, 6-month and 24-month results of QCA analysis.

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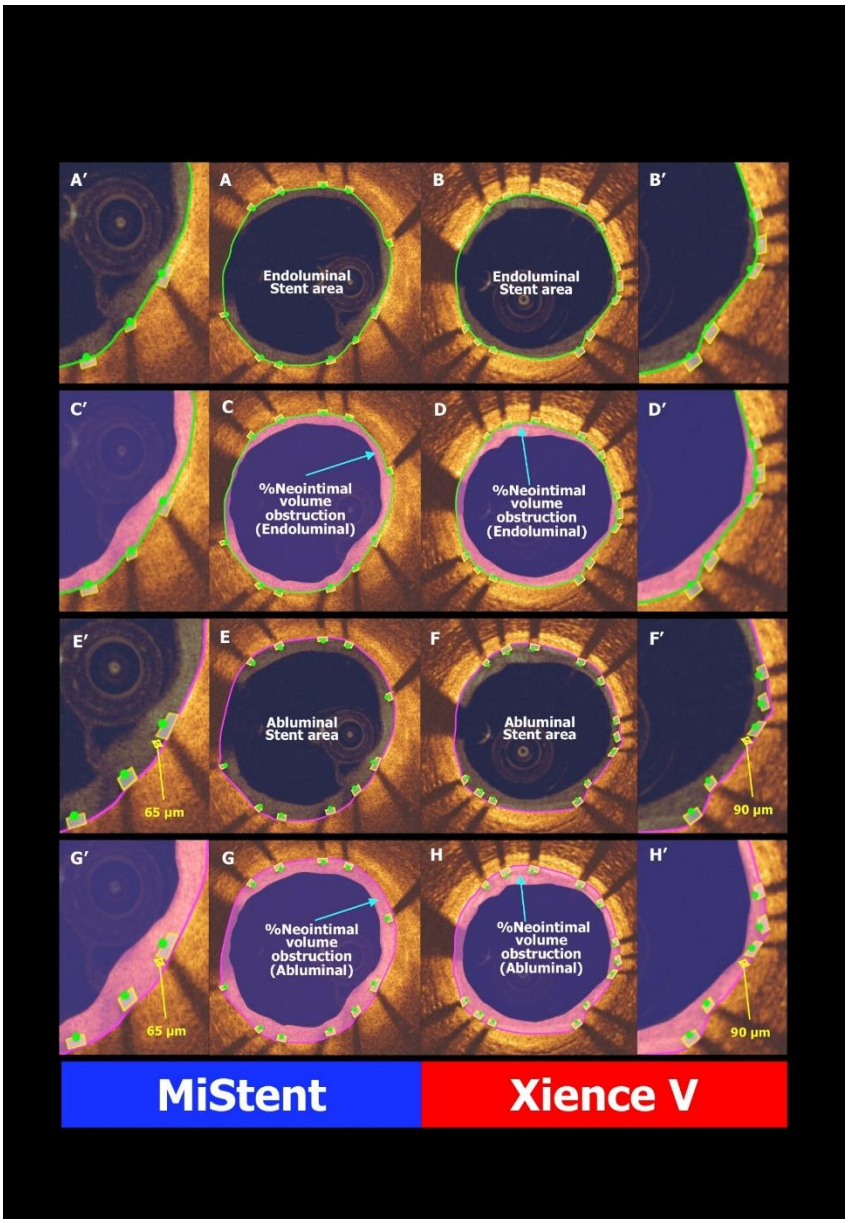
Supplementary data

Supplementary Appendix 1. The calculation method of the (modified) healing score on OCT assessment

The healing score is calculated based on four components (presence of filling defect [% intraluminal defect, ILD], both malapposed and uncovered struts [% malapposed/uncovered, MU], uncovered struts alone [% uncovered, U], and malapposed struts alone [% malapposed, M]); neointimal healing score=(%ILD*4)+(%MU*3)+(%U*2)+(%M*1). The modified healing score is calculated by addition of the value of the percentage volume obstruction (%VO) over 30% to the healing score and assigned a weight of 1; the modified neointimal healing score=(%ILD*4)+(%MU*3)+(%U*2)+(%M* 1)+(max(0,%VO>30)*1).

Supplementary Appendix 2. Statistical analysis

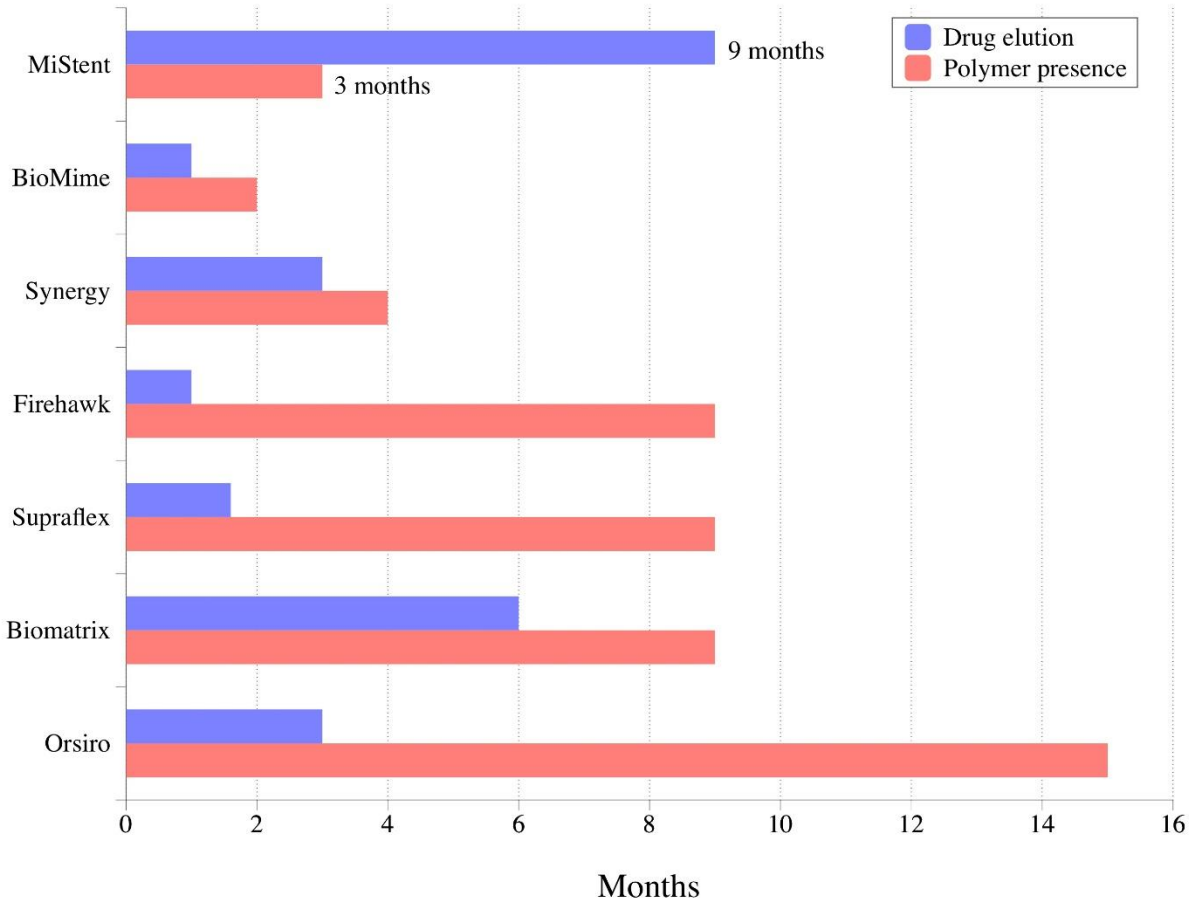
This is an observational and hypothesis-generating study without formal sample size calculation. The results are summarised per lesion. Continuous variables are presented as mean and standard deviation (SD), and compared using a two-sample t-test or Wilcoxon signed-rank test. Dichotomous variables are presented as percentages and numbers and compared using Pearson's chi-squared test or Fisher's exact test as appropriate. Two-sided p-values less than 0.05 are considered significant. Statistical analysis is performed by an independent research organisation (Cardialysis B.V., Rotterdam, the Netherlands), using SAS, versions 9.2 and 9.3 (SAS Institute Inc., Cary, NC, USA).



Supplementary Figure 1.

Endoluminal and abluminal assessment on OCT that delineates automatically either the endoluminal leading edge of the strut or the abluminal backside of the strut.

Endoluminal stent area, endoluminal % neointimal volume obstruction, abluminal stent area, and abluminal % neointimal volume obstruction are shown in A, C, E, G (MiStent) and B, D, F, H (XIENCE), respectively. A'-H' are magnified views of A-H.



Supplementary Figure 2. Time course for drug delivery and polymer degradation in various drug-eluting stents with bioresorbable coating.

Supplementary Table 1. Endoluminal quantitative OCT results at 6 and 24 months.

	6 months				24 months			
	MiStent (16 patients, 16 lesions)	**XIENCE (20 patients, 22 lesions)**	**Difference [95% CI]**	***p*-value**	**MiStent (16 patients, 16 lesions)**	**XIENCE (20 patients, 22 lesions)**	**Difference [95% CI]**	***p*-value**
Mean stent area, mm^2	6.12±1.53	6.23±1.74	-0.12 [-1.22, 0.99]	0.83	6.18±1.49	6.30±1.86	-0.12 [-1.26, 1.03]	0.84
Minimal stent area, mm^2	5.03±1.21	5.08±1.54	-0.04 [-0.98, 0.90]	0.93	4.97±1.18	5.13±1.68	-0.16 [-1.16, 0.83]	0.74
Mean neointimal hyperplasia area, mm^2	0.49±0.26	0.59±0.37	-0.10 [-0.32, 0.12]	0.35	0.90±0.49	0.86±0.33	0.05 [-0.22, 0.31]	0.74
Neointimal hyperplasia volume obstruction, %	7.88±3.68	9.93±6.20	-2.04 [-5.58, 1.49]	0.21	14.06±6.25	14.43±7.00	-0.37 [-4.83, 4.10]	0.87
Mean malapposition area, mm^2	0.08±0.22	0.04±0.10	0.04 [-0.07, 0.15]	0.51	0.06±0.19	0.02±0.05	0.04 [-0.05, 0.12]	0.44
Minimum stent eccentricity	0.80±0.09	0.84±0.05	-0.04 [-0.09, 0.00]	0.09	0.78±0.08	0.82±0.05	-0.04 [-0.09, 0.00]	0.054
Stent asymmetry index	0.27±0.08	0.25±0.07	0.02 [-0.03, 0.07]	0.46	0.30±0.08	0.26±0.09	0.04 [-0.02, 0.09]	0.17
Stent expansion	0.84±0.20 (15)	0.99±0.22 (21)	-0.15 [-0.29, -0.00]	0.046	0.91±0.26 (15)	1.08±0.37 (21)	-0.17 [-0.40, 0.06]	0.14
Minimal lumen eccentricity	0.73±0.08	0.74±0.07	-0.01 [-0.06, 0.04]	0.63	0.72±0.07	0.75±0.07	-0.03 [-0.08, 0.01]	0.17
Lumen asymmetry index	0.38±0.09	0.37±0.09	0.01 [-0.05, 0.08]	0.65	0.39±0.10	0.37±0.10	0.02 [-0.05, 0.08]	0.64
Healing score	1.71±3.42	0.67±1.32	1.04 [-0.57, 2.66]	0.2	3.86±6.12	2.93±5.29	0.93 [-2.84, 4.69]	0.62
Modified healing score	1.71±3.42	0.67±1.32	1.04 [-0.57, 2.66]	0.2	3.86±6.12	2.93±5.29	0.93 [-2.84, 4.69]	0.62

Data are presented as mean±standard deviation.

Supplementary Table 2. Baseline, 6-month and 24-month results of QCA analysis.

	MiStent (16 patients, 16 lesions)	XIENCE (20 patients, 22 lesions)	Difference [95% CI]	*p*-value
Pre-procedure				
Reference vessel diameter, mm	2.64±0.32	2.55±0.35	0.09 [-0.16, 0.34]	0.47
Minimum lumen diameter, mm	1.06±0.54	0.81±0.64	0.25 [-0.16, 0.66]	0.23
Percentage stenosis	60.6±18.6	67.5±25.8	-6.9 [-22.7, 8.8]	0.38
Obstruction length, mm	9.71±5.71	11.27±7.29	-1.56 [-6.51, 3.39]	0.52
Post-procedure				
Reference vessel diameter, mm	2.58±0.31	2.54±0.39	0.03 [-0.21, 0.28]	0.78
Minimum lumen diameter, mm	2.31±0.34	2.19±0.30	0.12 [-0.09, 0.34]	0.25
Percentage stenosis	10.5±7.6	13.5±6.6	-3.0 [-7.8, 1.8]	0.21
Acute gain, mm*	1.24±0.35	1.39±0.66	-0.15 [-0.59, 0.29]	0.42
6-month follow-up				
Reference vessel diameter, mm	2.52±0.30	2.47±0.34	0.05 [-0.18, 0.28]	0.68
Minimum lumen diameter, mm	2.28±0.24	2.07±0.36	0.21 [-0.02, 0.44]	0.07
In-stent percent diameter stenosis	9.1±5.0	16.2±10.1	-7.0 [-13.0, -1.0]	0.012
In-segment percent diameter stenosis	15.1±6.7	20.9±9.3	-5.8 [-11.7, 0.1]	0.054
Binary restenosis	0.0% (0/14)	0.0% (0/20)		
Late loss, mm**	0.02±0.31	0.18±0.24	-0.16 [-0.35, 0.03]	0.10
24-month follow-up				
Reference vessel diameter, mm	2.43±0.37	2.40±0.41	0.03 [-0.23, 0.29]	0.80
Minimum lumen diameter, mm	2.06±0.27	1.97±0.40	0.09 [-0.15, 0.33]	0.45
In-stent percent diameter stenosis	14.8±8.3	17.8±10.0	-3.1 [-9.3, 3.2]	0.32
In-segment percent diameter stenosis	18.4±9.3	22.2±10.1	-3.8 [-10.3, 2.7]	0.25
Binary restenosis	0.0% (0/16)	0.0% (0/22)		
Late loss (mm)***	0.26±0.32	0.23±0.32	0.03 [-0.19, 0.25]	0.76

Data are presented as mean±standard deviation or percentage (number of events).
* only matching orthogonal views pre procedure and post procedure were taken into account.
** including late loss based on non-matching orthogonal views post procedure and at 6-month follow-up.
*** including late loss based on non-matching orthogonal views post procedure and at 24-month follow-up.