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ORIGINAL RESEARCH

A Prospective Randomized Trial Comparing 2 Different Paclitaxel-Coated Balloons in De Novo Coronary Artery Disease

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ABSTRACT

BACKGROUND The Genoss paclitaxel-coated balloon (PCB) is a novel PCB with shellac and vitamin E as excipients, enhancing drug delivery to the target lesion and minimizing restenosis.

OBJECTIVES This study aimed to compare quantitative coronary angiographic outcomes at 6 months after treatment of de novo coronary artery disease (CAD) with 2 different types of PCBs.

METHODS This prospective, multicenter, noninferiority trial randomized 204 patients with chronic coronary syndrome or stabilized acute coronary syndrome to treatment with the shellac and vitamin E-based PCB or the reference PCB (SeQuent Please NEO) in a 1:1 ratio. The primary endpoint was noninferiority for the 6-month angiographic in-lesion late lumen loss.

RESULTS The 6-month in-lesion late lumen loss was 0.06 ± 0.38 mm with shellac and vitamin E-based PCB vs 0.09 ± 0.36 mm with reference PCB. The 1-sided 97.5% upper confidence limit of the difference was 0.08 mm, which was lower than the noninferiority limit of 0.15 mm, achieving noninferiority (P for noninferiority = 0.001). There was comparable late lumen enlargement (44.7% vs 42.7%; $P = 0.903$) and binary restenosis rates (3.2% vs 6.7%; $P = 0.442$) following treatment with shellac and vitamin E-based PCB and reference PCB, respectively. Both PCBs had similar 12-month rates of target vessel failure (3.0% in shellac and vitamin E-based PCB vs 4.3% in reference PCB; $P = 0.921$).

CONCLUSIONS The Genoss PCB, formulated with shellac and vitamin E as excipients, demonstrated angiographic outcomes comparable to a clinically proven PCB in the treatment of de novo CAD. (Compare the Safety and Efficacy of Genoss® DCB and SeQuent® Please NEO in Coronary De Novo Lesions; NCT05096442) (JACC Asia. 2025;5:15–24)

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ABBREVIATIONS AND ACRONYMS

CAD = coronary artery disease

DCB = drug-coated balloon

DES = drug-eluting stent(s)

LLL = late lumen loss

MI = myocardial infarction

MLD = minimal lumen diameter

PCB = paclitaxel-coated balloon

PCI = percutaneous coronary intervention

Drug-coated balloons (DCBs) are recommended for in-stent restenosis with a Class I, Level of Evidence: A recommendation in the European revascularization guidelines.[1] Growing clinical evidence also supports their role in treating de novo coronary lesions.[2-5] Paclitaxel is the most widely used drug for balloon coating because of its high lipophilic profile and potent antiproliferative effect,[6] resulting in effective inhibition of neointimal proliferation. Although most randomized studies comparing DCBs to alternative percutaneous coronary therapies focus on iopromide-based paclitaxel-coated balloon (PCB), there are alternative PCBs with different excipients available for clinical applications. Several prospective randomized studies have shown comparable angiographic and clinical outcomes among different types of DCBs for patients with coronary in-stent restenosis.[7,8] However, studies comparing the effectiveness of different types of PCBs in de novo lesions are limited.

Genoss PCB (GENOSS Co Ltd) is a new DCB with a different excipient, shellac plus vitamin E, which is designed to enhance drug delivery to the target lesion. A recent randomized study showed comparable angiographic results between this new PCB and iopromide-based PCB for the treatment of coronary in-stent restenosis.[8] The objective of this study was to investigate the efficacy and safety of the new shellac plus vitamin E-based PCB compared with the clinically proven iopromide-based PCB for the treatment of de novo coronary artery disease (CAD).

METHODS

STUDY DESIGN AND PATIENT POPULATION. The Genoss PCB study (Compare the Safety and Efficacy of Genoss DCB and SeQuent Please NEO in Coronary De Novo Lesions; NCT05096442) is a prospective, randomized, multicenter, open-label, noninferiority trial conducted in 10 university hospitals in South Korea (Supplemental Table 1). It enrolled 204 patients with chronic coronary syndrome or stabilized acute coronary syndrome who had at least 1 de novo coronary artery lesion. This lesion was defined as a reference vessel diameter estimated visually to be between 2.0 and 4.0 mm. Patients with significant coronary artery stenosis (>50% diameter stenosis on coronary angiography by visual estimation) were included. The full inclusion and exclusion criteria are shown in Supplemental Table 2. Patients were randomized 1:1 to treatment with the study device (Genoss PCB) or control device (SeQuent Please Neo). Concealed randomization was performed with the use of SAS software (version 9.4) using a stratified block randomization method. Randomization was stratified according to the trial center. Sealed randomization envelopes were then created and distributed to each trial center to secure the integrity of the randomization process. The protocol was approved by all ethics committees of all participating centers. The study complied with the Declaration of Helsinki and was approved by all institutional ethics committees. All patients provided written informed consent for participation in the trial. Study coordination, data management, and on-site monitoring support were provided by an independent contract research organization company (Synex Consulting Ltd). The study sponsor did not have any role in the analysis and interpretation of data or writing of the paper and did not participate in the decision to submit the paper for publication.

STUDY DEVICES. The experimental device is coated with 3 μg paclitaxel/mm^2 of balloon surface, utilizing wax-free shellac and vitamin E as excipients, which is designed to enhance drug delivery to the target lesion and prevent restenosis. The control device is an iopromide-based DCB that is coated with 3 μg paclitaxel/mm^2 of balloon surface and uses iopromide as a hydrophilic excipient. It has been widely studied in clinical trials and has comparable data in de novo CAD when compared with drug-eluting stents (DES).

PROCEDURES. The predilation was performed according to the international and Asia-Pacific consensus recommendations for DCB treatment, using a conventional balloon with the recommended balloon-to-vessel ratio of 0.8 to 1.0 in all lesions.[9,10] Predilatation was considered successful, as assessed by the investigators, with a TIMI flow grade 3 regardless of dissection severity and by the absence of residual diameter stenosis >30%.[9,10] Only lesions having undergone successful predilatation (n = 204)

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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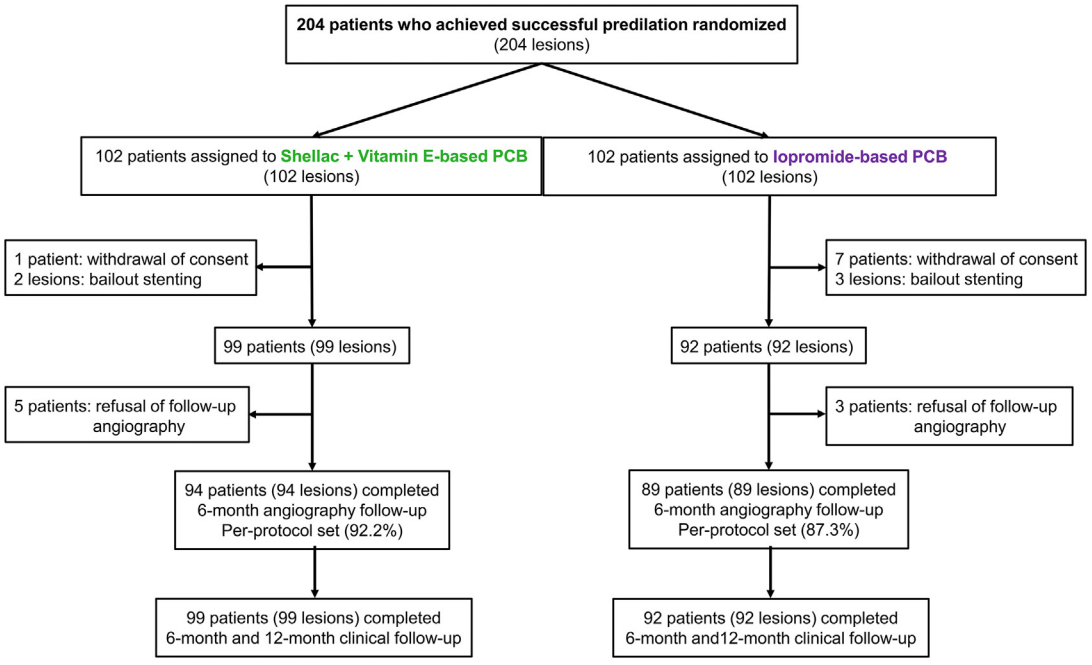
FIGURE 1 Flow Chart of the Study



From September 30, 2021, to November 14, 2022, 204 patients with de novo coronary artery disease were randomly assigned to either the shellac plus vitamin E-based paclitaxel-coated balloon (PCB) (n = 102) or the iopromide-based PCB (n = 102) treatment group.

were randomized. The recommended DCB balloon inflation time was at least 60 seconds with nominal pressure, but if the patient cannot tolerate this duration, inflation was performed twice for 30 seconds. After DCB use, the final assessment was performed at least 5 minutes after administering a bolus of an intracoronary vasodilator, to prevent any remaining acute vessel closure. All patients were preloaded with clopidogrel, ticagrelor, or prasugrel and were already taking aspirin before the procedure. Unfractionated heparin was administered according to the standard hospital practice. The duration of the prescribed dual antiplatelet therapy was at the discretion of the attending physician.

QUANTITATIVE CORONARY ANGIOGRAPHIC ASSESSMENTS. Angiography before and after all interventions and at angiographic follow-up was performed using identical projections and analyses off-line using validated Medis software (Medis QAngio, Medis). All coronary angiographic images were analyzed by an expert, who was blinded to clinical and randomization information, at the core laboratory of the Ulsan University Hospital. Measurements were obtained in the treated area using shoulder-to-shoulder measurement (in-lesion and reference segments were automatically identified by the system). The following parameters were analyzed: reference vessel diameter (RVD), minimal lumen diameter (MLD), percent diameter stenosis, acute lumen gain (MLD at post-DCB − MLD at baseline), late lumen loss (LLL) (MLD at post-DCB − MLD at 6-month follow-up), net lumen gain (MLD at 6-month follow-up − MLD at baseline), late lumen enlargement (− value of LLL), lesion length, binary restenosis (percent diameter stenosis ≥50% at follow-up), and severity of dissection (National Heart, Lung, and Blood Institute classification).

STUDY ENDPOINTS. The primary endpoint was an angiographic in-lesion LLL (mm) that was inside the DCB-treated area in the per-protocol population, which consisted of patients who received the assigned treatment in the absence of bail-out stenting. Prespecified secondary endpoints were target vessel failure composed of the occurrence of cardiac death, target vessel-related myocardial infarction (MI) (excluding periprocedural MI), and clinically and/or physiologically indicated target vessel revascularization (TVR) at 6 and 12 months. All clinical endpoints and adverse events were evaluated with the consensus of the investigators, and all events were cross-checked with the medical records by

TABLE 1 Baseline Clinical Characteristics

	Shellac + Vitamin E-Based PCB (n = 102)	Iopromide-Based PCB (n = 102)
Age, y	64.0 (56.0-71.0)	63.0 (58.0-67.0)
Male	85 (83.3)	86 (84.3)
Body mass index, kg/m^2	24.7 (22.9-26.5)	24.6 (23.2-27.0)
Hypertension	67 (65.7)	70 (68.6)
Diabetes mellitus	38 (37.3)	39 (38.2)
Dyslipidemia	64 (62.7)	62 (60.8)
Current smoker	22 (21.6)	31 (30.4)
Previous MI	5 (4.9)	4 (3.9)
Previous PCI	3 (2.9)	2 (2.0)
Previous CABG	0	0
Previous stroke	1 (1.0)	0
Clinical status		
Stable angina	51 (50.0)	48 (47.1)
Unstable angina	50 (49.0)	49 (48.0)
NSTEMI	1 (1.0)	5 (4.9)
CCS class		
I	56 (54.9)	59 (57.8)
II	39 (38.2)	37 (36.3)
III	5 (4.9)	2 (2.0)
IV	2 (2.0)	4 (3.9)
LVEF	60.8 ± 8.6	59.4 ± 7.4

Values are median (Q1-Q3), n (%), or mean ± SD.

CABG = coronary artery bypass graft; CCS = Canadian Cardiovascular Society; LVEF = left ventricular ejection fraction; MI = myocardial infarction; NSTEMI = non-ST-segment elevation myocardial infarction; PCB = paclitaxel-coated balloon; PCI = percutaneous coronary intervention.

external monitors. Given the different packaging of the study devices, the investigators performing the study procedures were not blinded to the treatment assignment; however, statisticians were blinded.

Periprocedural MI was defined according to the Society for Cardiovascular Angiography and Interventions 2013 definition and spontaneous MI according to the fourth universal definition.[11] A clinically relevant MI postprocedure is diagnosed by a new biomarker elevation of creatine kinase-myoglobin binding to ≥10× upper limit of normal or by creatine kinase-myoglobin binding to ≥5× upper limit of normal plus the development of new pathologic Q-waves in ≥2 contiguous leads or left bundle branch block.

STATISTICAL ANALYSIS. The study hypothesis was that the experimental device was noninferior to the control device for the treatment of de novo CAD, in terms of in-lesion LLL at the 6-month angiographic follow-up. A mean LLL of 0.01 ± 0.34 mm was expected in both device groups based on the LLL observed at 6 months in lesions treated with the iopromide-based PCB in a previous study.[12] Using a noninferiority margin of 0.15 mm and assuming an attrition rate of 20%, 102 patients per arm were required to achieve 80% power to demonstrate noninferiority with a 1-sided type error of 0.025.

For the demographic information, continuous data were summarized by descriptive statistics (number of subjects, mean ± SD, median [Q1-Q3]) and categorical data by frequency and fraction. Group comparisons used the Student's *t*-test or Mann-Whitney *U* test for continuous variables and the chi-square test or Fisher exact test for categorical variables. The linear regression models and Pearson correlation coefficient were used to estimate the association between acute lumen gain and net lumen gain. The 95% CIs for the coefficients of the linear model were plotted. The Cochran-Armitage test for trend was used to determine the relationship between the late lumen enlargement and RVD. All statistical analyses were performed at a 2-sided significance level of 0.05, using SPSS version 21.0 (IBM Corp), NCSS (NCSS LLC), and R version 4.3.2 (R Foundation for Statistical Computing).

RESULTS

From September 30, 2021, to November 14, 2022, 204 patients with de novo CAD were randomly assigned to either the shellac plus vitamin E-based PCB (n = 102) or the iopromide-based PCB (n = 102) treatment group. Figure 1 shows the flowchart of the trial. Baseline clinical characteristics are presented in Table 1. The median age was 64 years of age in the shellac plus vitamin E-based PCB and 63 years of age in the control group, and the majority were men. Baseline characteristics between the 2 groups were generally balanced, with no significant differences. Table 2 summarizes the lesion and procedural characteristics. The time for DCB delivery to the lesion and the duration for DCB inflation in both groups were comparable. The diameter of the DCB used was 2.80 ± 0.45 mm in the shellac plus vitamin E-based PCB and 2.83 ± 0.45 mm in the control, with no difference. When compared with RVD after predilation, the DCB to artery ratio was the same at 1.1 ± 0.1 in both groups. After DCB treatment, severe dissection (≥ type C) was comparable in both groups (6.9% [7 of 102] in shellac plus vitamin E-based PCB vs 7.8% [8 of 102] in the control group). Bailout stenting occurred in 2.0% [2 of 102] of the shellac plus vitamin

E-based PCB group and 2.9% [3 of 102] in the control group. There were 60 lesions (29.4% [60 of 204]) with a reference vessel diameter exceeding 2.75 mm, and 39 lesions (19.1% [39 of 204]) with a reference vessel diameter of 3.0 mm or greater.

ANGIOGRAPHIC OUTCOMES. Table 3 summarizes the serial quantitative coronary angiographic results. The 6-month in-lesion LLL was 0.06 ± 0.38 mm (median 0.06 mm [Q1-Q3: −0.16 to 0.20 mm]) with shellac plus vitamin E-based PCB compared with 0.09 ± 0.36 mm (median 0.04 mm [Q1-Q3: −0.16 to 0.32 mm]) with iopromide-based PCB ($P = 0.561$). The upper limit of the 97.5% 1-sided CI for differences was 0.08 mm, lower than the noninferiority limit of 0.15 mm, achieving the noninferiority of shellac plus vitamin E-based PCB to iopromide-based PCB (P for noninferiority = 0.001).

Baseline angiographic parameters, lesion length, RVD, MLD, and percent diameter stenosis, did not differ between the groups. After DCB treatment, there were comparable increases in RVD and MLD, and decreased percent diameter stenosis in both groups. Acute lumen gain was 1.07 ± 0.36 mm in shellac plus vitamin E-based PCB vs 1.13 ± 0.41 mm in control ($P = 0.301$). At the 6-month angiographic follow-up, there were no significant differences observed between the 2 groups. Net lumen gain (1.02 ± 0.49 mm vs 1.04 ± 0.49 mm; $P = 0.739$) and late lumen enlargement (44.7% [42 of 94] vs 42.7% [38 of 89]; $P = 0.903$) were similar in the shellac plus vitamin E-based PCB and control group, respectively. As shown in Table 3, no significant difference between the 2 groups were noted in binary restenosis (3.2% [3 of 94] in the shellac plus vitamin E-based PCB vs 6.7% [6 of 89] in the control group; $P = 0.442$). At the follow-up angiography, no instances of aneurysmal formation were observed in the lesions treated with either DCB. Figure 2 presents the cumulative frequency distributions of in-lesion MLD and percent diameter stenosis. Figure 3 shows the cumulative frequency distributions of in-lesion LLL, late lumen enlargement, and net lumen gain. The greater the acute lumen gain after DCB treatment in index percutaneous coronary intervention (PCI), the greater the net lumen gain in follow-up, which was similar in both groups (Supplemental Figure 1).

CLINICAL OUTCOMES. Clinical follow-up was completed for all patients in both groups at 6 and 12 months. Table 4 summarizes the clinical events in hospital, at 6 and 12 months. There was no death and acute vessel closure in the hospital period.

TABLE 2 Lesion and Procedural Characteristics

	Shellac + Vitamin E-Based PCB (n = 102)	Iopromide-Based PCB (n = 102)	*P* Value
Target vessel location			0.142
Left anterior descending artery	40 (39.2)	38 (37.3)	
Diagonal branch	9 (8.8)	3 (2.9)	
Left circumflex artery	26 (25.5)	28 (27.5)	
Obtuse marginal branch/ramus	11 (10.8)	9 (8.8)	
Right coronary artery	11 (10.8)	22 (21.6)	
PDA/PL	5 (4.9)	2 (2.0)	
Bifurcation	48 (47.1)	48 (47.1)	>0.999
Target lesion, AHA type B2/C	54 (52.9)	57 (55.9)	0.779
Balloon predilation	102 (100.0)	102 (100.0)	>0.999
Type of predilation balloon			0.342
Semicompliant	48 (47.1)	47 (46.1)	
Noncompliant	34 (33.3)	27 (26.5)	
Scoring balloon	20 (19.6)	28 (27.5)	
Successful delivery of DCB	102 (100.0)	102 (100.0)	>0.999
DCB delivery time, s	29.0 ± 34.6	28.6 ± 35.3	0.942
DCB inflation duration, s	58.1 ± 7.9	57.6 ± 9.0	0.645
Number of DCBs	1.0 (1.0-1.0)	1.0 (1.0-1.0)	0.248
DCB diameter	2.80 ± 0.45	2.83 ± 0.45	0.613
Number of DCB diameters ≥3.0 mm	36 (35.3)	40 (39.2)	0.664
DCB length	25.2 ± 5.0	25.4 ± 5.2	0.839
Maximal DCB pressure, atm	8.7 ± 1.7	8.2 ± 2.3	0.079
DCB to artery ratio	1.1 ± 0.1	1.1 ± 0.1	0.865
Intravascular imaging used			
IVUS	32 (31.4)	28 (27.5)	0.645
OCT	18 (17.6)	23 (22.5)	0.485
Dissection type after DCB treatment			0.807
None	60 (58.8)	62 (60.8)	
A	19 (18.6)	14 (13.7)	
B	16 (15.7)	18 (17.6)	
C	7 (6.9)	8 (7.8)	
TIMI flow grade 3 after procedure	101 (99.0)	100 (98.0)	0.605
Bailout stenting	2 (2.0)	3 (2.9)	>0.999

Values are n (%), mean ± SD, or median (Q1-Q3).

AHA = American Heart Association; DCB = drug-coated balloon; IVUS = intravascular ultrasound; OCT = optical coherence tomography; PCB = paclitaxel-coated balloon; PDA = posterior descending artery; PL = posterolateral artery.

Periprocedural MI was comparable between both groups (4.0% [4 of 99] in the shellac plus vitamin E-based PCB vs 6.5% [6 of 92] in the control group; $P = 0.776$). There were no deaths or cardiac deaths at the 6-month follow-up. The TLR rates were not significantly different between both groups at 6 and 12 months (3.0% [3 of 99] in the shellac plus vitamin E-based PCB group vs 4.3% [4 of 92] in the control group; $P = 0.921$). After 6 months, 1 patient in the shellac plus vitamin E-based PCB group experienced a target vessel MI caused by target lesion thrombosis, and 1 death occurred in the control group.

TABLE 3 Serial Quantitative Coronary Angiographic Results

	Shellac + Vitamin E-Based PCB (n = 94)	Iopromide-Based PCB (n = 89)	*P* Value
Before procedure			
Lesion length, mm	16.8 ± 6.5	16.9 ± 6.5	0.913
Reference vessel diameter, mm	2.45 ± 0.52	2.50 ± 0.58	0.503
Minimal lumen diameter, mm	0.89 ± 0.38	0.83 ± 0.40	0.269
Diameter stenosis, %	64.3 ± 12.1	67.5 ± 12.9	0.072
After DCB treatment			
Reference vessel diameter, mm	2.62 ± 0.49	2.67 ± 0.52	0.546
Minimal lumen diameter, mm	1.97 ± 0.44	1.96 ± 0.45	0.933
Diameter stenosis, %	25.0 ± 8.7	26.5 ± 7.6	0.195
Acute lumen gain, mm	1.07 ± 0.36	1.13 ± 0.41	0.301
At 6-mo			
Reference vessel diameter, mm	2.61 ± 0.54	2.66 ± 0.58	0.561
Minimal lumen diameter, mm	1.93 ± 0.58	1.88 ± 0.58	0.581
Diameter stenosis, %	27.0 ± 13.9	30.2 ± 12.9	0.112
Late lumen loss, mm	0.06 ± 0.38	0.09 ± 0.36	0.561
Net lumen gain, mm	1.02 ± 0.49	1.04 ± 0.49	0.739
Late lumen enlargement, %	42 (44.7)	38 (42.7)	0.903
Binary restenosis	3 (3.2)	6 (6.7)	0.442
Aneurysmal formation in treated lesions	0	0	–

Values are mean ± SD or n (%).
Abbreviations as in Table 2.

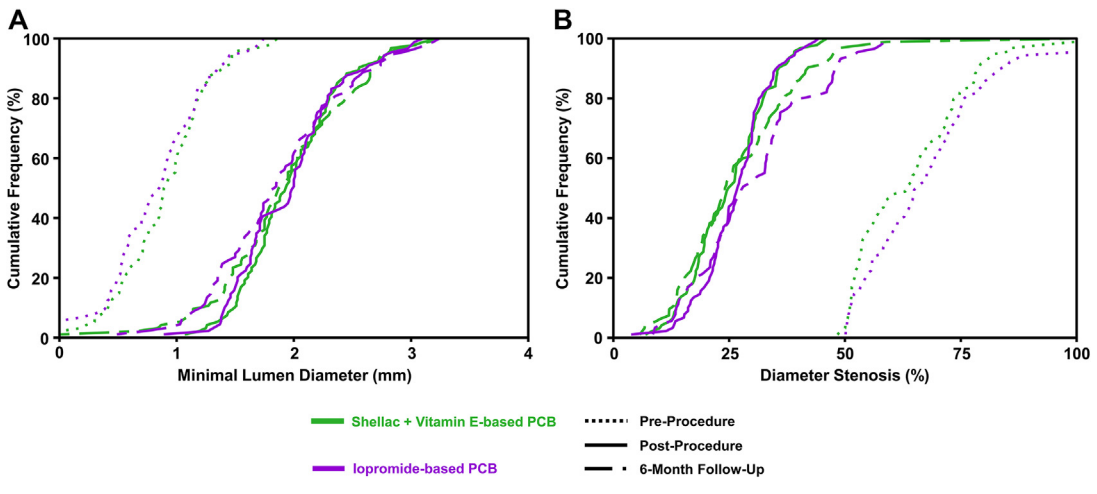
DISCUSSION

This trial demonstrated that the shellac plus vitamin E-based PCB was noninferior to the iopromide-based PCB with regard to the primary endpoint of 6-month in-lesion LLL in treating de novo CAD. Additionally, the rates of adverse clinical events within 6 and 12 months were comparable between the treatment groups. The results of this statistically powered head-to-head randomized trial comparing 2 different PCBs add important insights to the available clinical evidence for the treatment strategies for de novo CAD (Central Illustration).

Although new-generation DES have shown significant improvements in reducing adverse events compared with bare-metal stents and first-generation DES, contemporary DES still carry risks of short- and long-term stent-related adverse events because of their permanent metallic cage.[13-15] Additionally, stent implantation can impair restoration of vasomotion in stented segments[16] and accelerate neoatherosclerosis compared with native coronary lesions.[17] The increasing clinical evidence supports the efficacy of DCBs in the treatment of de novo CAD.[3,5,18-20] Many randomized studies comparing DCBs with alternative percutaneous therapies for de novo CAD are based on data from the iopromide-based PCB.[2,4,21,22]

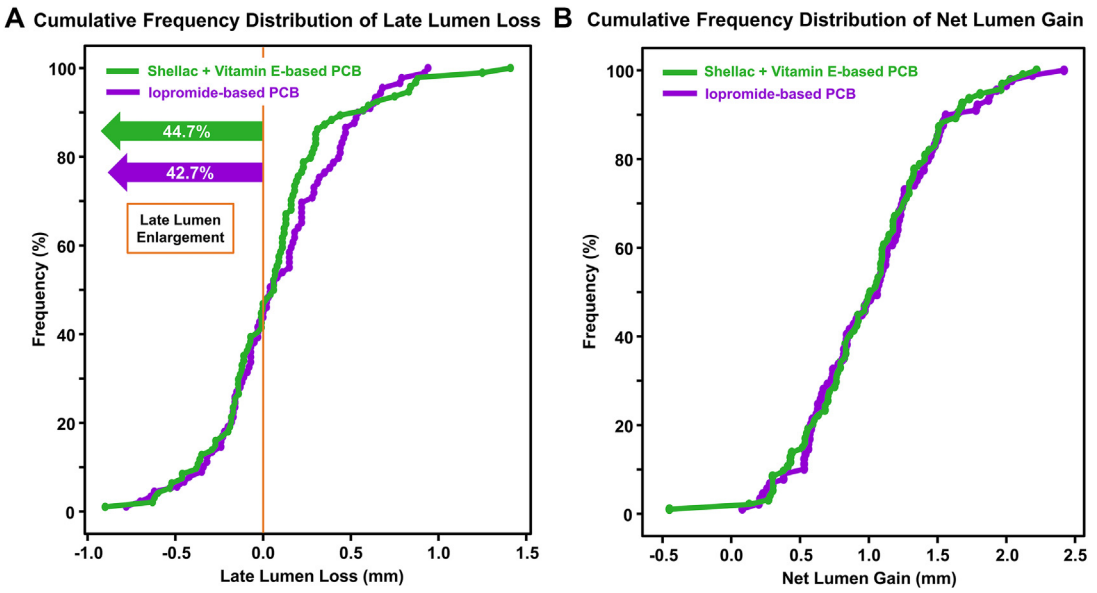
The shellac plus vitamin E-based PCB surface is coated with shellac, which is a hydrophilic substance for rapid release and diffusion into the tissue.[23] Added to the coating is the antioxidant vitamin E, which is known to be effective in preventing restenosis by reducing local plasminogen activator inhibitor-1 and by directly blocking the accumulation of smooth muscle cells, which are activated when the vascular wall is damaged after balloon angioplasty.[24]

FIGURE 2 Cumulative Frequency Distribution of Minimal Lumen Diameter and Diameter Stenosis



Cumulative frequency distribution curve of (A) minimal lumen diameter and (B) diameter stenosis, respectively. The cumulative frequency distributions of in-lesion minimal lumen diameter and percent diameter stenosis show comparable results between the 2 groups.
PCB = paclitaxel-coated balloon.

FIGURE 3 Cumulative Frequency Distribution of In-Lesion Lumen Loss and Lumen Gain



Cumulative frequency distribution curve of (A) late lumen loss and (B) net lumen gain, respectively. The cumulative frequency distribution curves of late lumen loss and net lumen gain show comparable results between the 2 groups. PCB = paclitaxel-coated balloon.

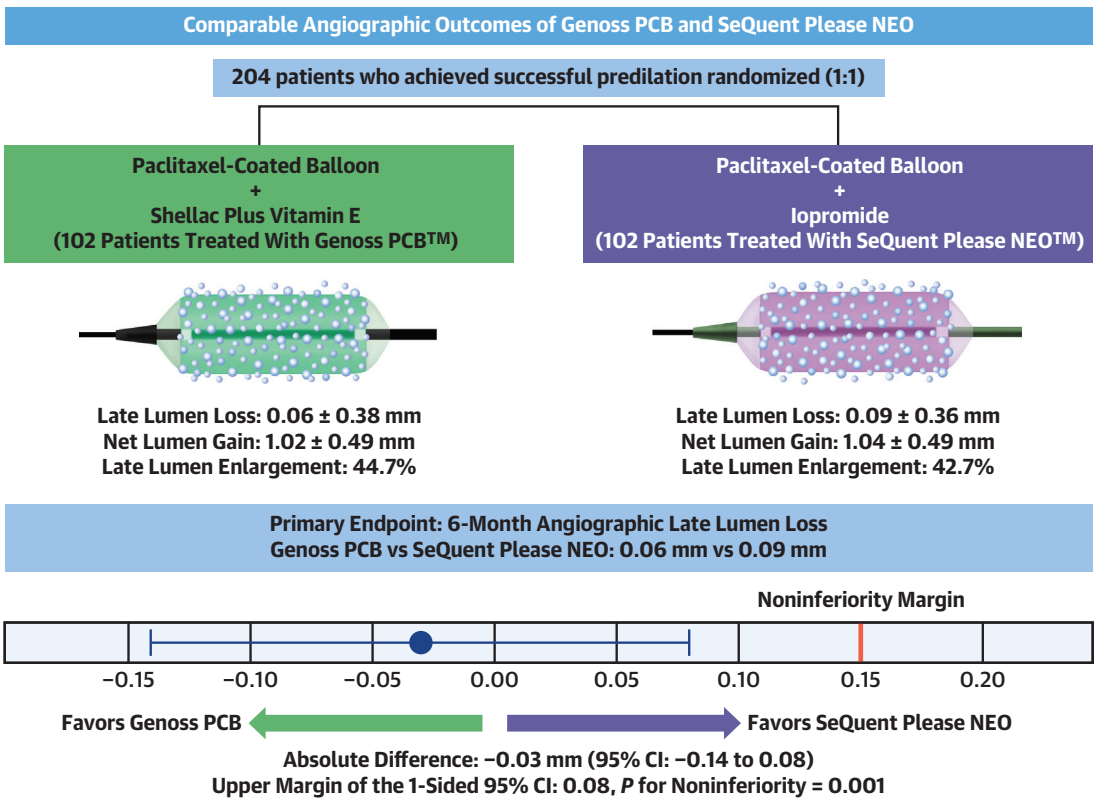
In a previous study, the shellac plus vitamin E-based PCB showed a comparable result to the iopromide-based PCB for the primary endpoint of 6-month LLL for the treatment of coronary in-stent restenosis.[8] A total of 82 patients from 7 centers were randomized, and the 6-month LLL was 0.15 ± 0.43 mm with the shellac plus vitamin E-based PCB compared with 0.24 ± 0.39 mm with the iopromide-based PCB. The 1-sided 97.5% upper confidence limit of the difference was 0.13 mm, lower than the noninferiority limit of 0.29 mm, achieving noninferiority (*P* for noninferiority = 0.001). Major cardiovascular events were comparable between 2 groups at 6 months (7.7% for the shellac plus vitamin E-based DCB vs 10.3% for the iopromide-based PCB; *P* = 0.692). Furthermore, this trial is the first to compare the effectiveness of shellac plus vitamin E-based PCB with iopromide-based PCB in de novo coronary lesions. The study PCB, formulated with shellac and vitamin E as excipients, demonstrated angiographic outcomes comparable to those of a clinically proven PCB in treating de novo CAD. This establishes that shellac plus vitamin E-based PCB exhibits angiographic noninferiority compared with iopromide-based PCB, not

TABLE 4 Clinical Outcomes

	Shellac + Vitamin E-Based PCB (n = 99)	Iopromide-Based PCB (n = 92)	*P* Value
In hospital			
Death	0	0	–
Acute vessel closure	0	0	–
Periprocedural myocardial infarction	4 (4.0)	6 (6.5)	0.776
At 6-mo follow-up			
Death	0	0	–
Cardiac death	0	0	–
Target vessel myocardial infarction	0	0	–
Target lesion thrombosis	0	0	–
Target lesion revascularization	1 (1.0)	3 (3.3)	0.562
Target vessel revascularization	1 (1.0)	3 (3.3)	0.562
At 12-mo follow-up			
Death	0	1 (1.0)	–
Cardiac death	0	0	–
Target vessel myocardial infarction	1 (1.0)	0	–
Target lesion thrombosis	1 (1.0)	0	–
Target lesion revascularization	3 (3.0)	4 (4.3)	0.921
Target vessel revascularization	3 (3.0)	4 (4.3)	0.921

Values are n (%).
PCB = paclitaxel-coated balloon.

CENTRAL ILLUSTRATION **A Prospective, Randomized Multicenter, Noninferiority Trial in De Novo CAD**



The 6-month in-lesion late lumen loss was 0.06 ± 0.38 mm with shellac plus vitamin E-based paclitaxel-coated balloon (PCB) (Genoss PCB) vs 0.09 ± 0.36 mm with reference PCB (SeQuent Please NEO). The 1-sided 97.5% upper confidence limit of the difference was 0.08 mm, lower than the noninferiority limit of 0.15 mm, achieving noninferiority (*P* for noninferiority = 0.001). CAD = coronary artery disease.

only in in-stent restenosis lesions but also in de novo coronary lesions.

One of the interesting aspects of this study is that it shows the importance of balloon angioplasty in index PCI. Supplemental Figure 1 shows that the acute lumen gain obtained after PCI is highly correlated with the net lumen gain after 6 months. In other words, this suggests that obtaining sufficient lumen gain through balloon angioplasty can improve angiographic outcomes in the future. Because the basis of DCB treatment is balloon angioplasty, efforts must be made to achieve an appropriate lumen gain during the index PCI. Another interesting aspect in this study is that a larger RVD tends to result in greater late lumen enlargement after DCB treatment. We are conducting a study comparing the safety and effectiveness of DCB with DES for large vessel disease (RVD ≥3.0 mm). The results of this study, known as the REVERSE (Drug-Coated Balloon vs. Drug-Eluting Stent for Clinical Outcomes in Patients With Large Coronary Artery Disease; NCT05846893) trial, are expected to provide insights into clinical outcomes in de novo large vessel CAD.

The results of this new head-to-head comparison randomized trial, evaluating 2 different PCBs in de novo CAD, provide important insights into the available clinical evidence for treatment strategies in de novo CAD. To our knowledge, this is the first evidence that shellac plus vitamin E-based PCB is effective and safe, at least for the treatment of de novo CAD at the 6-month follow-up.

STUDY LIMITATIONS. First, it was challenging to ensure sufficient power to detect differences in clinical outcomes caused by the relatively low sample size. As a result, no further conclusions can be drawn regarding the clinical safety or efficacy of shellac plus vitamin E-based PCB. However, angiographic surrogate endpoints such as LLL have been widely used and validated in other trials assessing the safety and efficacy of DCB. Real-world evidence and randomized trials, powered for clinical outcomes, are important to confirm the clinical effectiveness of the shellac plus vitamin E-based PCB.

CONCLUSIONS

In this multicenter, head-to-head noninferiority randomized trial, Genoss PCB, formulated with shellac and vitamin E as excipients, demonstrated angiographic outcomes comparable to those of a clinically proven PCB in the treatment of de novo CAD.

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APPENDIX For supplemental tables and a figure, please see the online version of this paper.