A Small scale, Prospective, Multicenter, Single arm, Investigator-initiated Feasibility Clinical Study to Evaluate the Efficacy and Safety of Paclitaxel Coated PTCA Balloon Catheter (GENOSS® DCB) in Patients with De novo lesion of Coronary Artery

Protocol No.: CEP-DS1001_FS

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CONFIDENTIAL

[Clinical trial protocol enactment and revision history]

No.	Version No.	Version Date	주요 변경내용
1	1.0	16Aug2022	N/A
2	1.1	14Oct2022	Correct errors (delete random assignment, test group, control group, blinding, independent evaluator), insert single group, Investigator-initiated text, modify test method

[Index]

[SUMMARY OF CLINICAL TRIAL]

Clinical trial title	A Small scale, Prospective, Multicenter, Single arm, Investigator-Initiated Feasibility Clinical Study to Evaluate the Efficacy and Safety of Paclitaxel Coated PTCA Balloon Catheter (GENOSS® DCB) in Patients with De novo lesion of coronary artery
Clinical trial purpose	GENOSS® DCB, Paclitaxel Coated PTCA Balloon Catheter, has received approval from the Ministry of Food and Drug Safety for in-stent restenosis (ISR), but has not been evaluated for new lesions. Therefore, in this study, We aim to evaluate clinical feasibility through a small-scale, multi-center, single-group, investigator-initiated pilot study targeting patients with de novo lesions measuring 2.0 mm to 4.0 mm in diameter.
Coordinating investigator	Hallym university Kangnam sacred heart hospital / Professor Jung Rae Cho (Department of Cardiology)
Clinical trial institution / Principal investigator	■ Hallym University Kangnam Sacred Heart Hospital / Professor Jung Rae Cho (Department of Cardiology) ■ Severance Hospital / Professor Jung Sun Kim (Cardiology)
Sponsor	Hallym University Kangnam Sacred Heart Hospital (07441) 1 Singil-ro, Yeongdeungpo-gu, Seoul (Daerim-dong 948-1)
Investigational device	■ Medical device for testing Genoss® DCB (A57130.21[class 4], Approval No. 20-501, Paclitaxel Coated PTCA Balloon Catheter, Manufacturer: Genos Co., Ltd., Model name : GDEB-10-200 and 161 other cases) Previous/approved purpose of use: A balloon catheter used in percutaneous coronary intervention (PCI) for the treatment of in-stent restenosis due to late lumen loss of stents with a reference vessel diameter of 2.0 mm to 4.0 mm.
Clinical trial period	Approximately 21 months after approval from the Ministry of Food and Drug Safety/ Institutional Review Board of the clinical trial After obtaining approval for the clinical trial plan from the Ministry of Food and Drug Safety's Institutional Review Board, it is expected to take approximately 21 months, including 3 months for IRB approval, 12 months for subject recruitment, and 6 months for follow-up. Even after the clinical trial is completed, it is expected to take approximately 5 additional months for data processing, statistical analysis, preparation of Clinical study report,

	and submission to the Institutional Review Board.
Target disease	Patients who need intervention due to a de-novo lesion in a coronary artery with a diameter of 2.0 mm to 4.0 mm
Number of subjects	Total 20 (10 at Hallym University Kangnam Sacred Heart Hospital, 10 at Severance Hospital)
Inclusion criteria	You must meet all of the following inclusion criteria to be registered in this clinical trial. **Inclusion criteria:** 1. Adults over 19 years old 2. When intervention is required due to a new lesion in the coronary artery* ** Coronary artery lesion that has never been treated with any interventional procedure (e.g., plain old balloon angioplasty (POBA), stent, rotablation, laser procedure, etc.)* 3. In case of stable angina, unstable angina, or silent ischemia 4. If you are a woman of childbearing age, you agree to use one or more clinically appropriate contraceptive methods* during the test period. ** Clinically appropriate contraception is defined as "[an intrauterine device (e.g. loop, Mirena), chemical barrier method (spermicide), or subcutaneous implant contraceptive device (e.g. Implanon)] plus a physical barrier method (male or female), tubal surgery, or laparoscopic contraception(a type of tubal ligation).* 5. A person who voluntarily agrees to participate in a clinical trial and is willing to comply with the subject compliance requirements **Inclusion criteria in coronary angiography:** 1. If there is significant coronary artery stenosis (>50% diameter stenosis on coronary angiography) 2. When the length of the lesion on coronary angiography is less than 34 mm and the reference vessel diameter of the coronary artery is between 2.0 mm and 4.0 mm.
Exclusion criteria	If you meet any of the following exclusion criteria, you cannot be registered for a clinical trial. **Exclusion criteria:** 1. Persons with ST segment elevation myocardial infarction (STEMI) 2. Persons with known hypersensitivity or contraindications to the following drugs or substances • aspirin, • clopidogrel

	• heparin, • Prasugrel • Ticagrelor • paclitaxel • Contrast media (Iopromide, etc.) *(However, even subjects with hypersensitivity to contrast media can be registered if they can be controlled with steroids and pheniramine, but cases with known anaphylaxis are excluded)* 3. Patients with platelet aggregation or disorders at risk of increased bleeding, such as gastrointestinal ulcers, which limit platelet aggregation inhibitor therapy and anticoagulant therapy. 4. Patients with left ventricular ejection fraction less than 30% according to echocardiography. 5. Cases not suitable for coronary angiography due to current or past severe renal failure (eGFR < 30 ㎖/min) 6. In case of cardiogenic shock 7. If you are pregnant or lactating 8. If the life expectancy is less than 1 year due to a concomitant disease 9. If you have had or currently have a medical illness such as mental illness that significantly affects this clinical trial. 10. If, in the judgment of the investigator, it is not suitable for this clinical trial or may increase the risks associated with participation in the study 11. Those who are currently participating in another clinical trial or have participated in another clinical trial within 90 days of the screening date 12. In other cases, when the investigator determines that participation in the clinical trial is inappropriate because it may affect the results of the clinical trial or ethically. ☞ *Specific reasons are stated in the case report form.* **<u>Exclusion criteria in Coronary angiography:</u>** 13. In case of graft vessel lesion 14. In case of left main coronary lesion 15. When it is difficult to apply an investigational device because pre-expansion is not possible or pre-expansion fails 16. If one of the following items applies after pre-expansion of the target lesion: ① When measured as FFR (Functional measurement) ≤ 0.8 in a large vessel (limited to cases with a diameter of 3.0 mm or more) (However, FFR measurement may not be performed at the discretion of the researcher.) ② Those who need stent surgery due to vascular dissection that restricts blood flow ③ When residual stenosis is > 30%

	④ When TIMI flow is < 3
Clinical trial design	A Small scale, Prospective, Multicenter, pilot study
Clinical trial method	1. Patients who are deemed to require interventional procedures due to a de novo lesion in the coronary artery are referred to this clinical trial. 2. Those who voluntarily sign a written consent form after receiving a sufficient explanation of the clinical trial will undergo a screening test. 3. Excluding the selection/exclusion criteria that require confirmation on the day of the procedure through a screening test, Potential subjects who meet all selection/exclusion criteria (items that can be confirmed by coronary angiography and whether pre-dilatation is successful or not are confirmed on the procedure day) are checked on the date of hospitalization and the procedure. Make a reservation and be hospitalized on the scheduled date to receive pre-procedure treatment and drug therapy (aspirin and P2Y12 inhibitors) (Generally, patients are hospitalized the day before the procedure, but the hospitalization date can be changed at the discretion of the investigator.)) 4. On the day of the procedure, the selection/exclusion criteria for the lesion are confirmed through coronary angiography, and pre-dilation is performed according to the procedure below. ※ *If there are two or more lesions that meet the inclusion criteria, the lesion with the narrowest minimum lumen diameter is selected as the target lesion.* * Pre-dilation: This is a procedure to expand the target lesion using a standard balloon that is not coated with drugs before the DCB procedure. Apply DCB after completely improving the plaque of the lesion with a standard balloon of optimal size (balloon to artery ratio 1:1). If expansion of a standard semi-compliant balloon fails, a high-pressure non-compliant balloon or a cutting and scoring balloon is recommended. 5. If pre-dilation was not performed or pre-dilation failed, or if vascular dissection (exclusion criteria 17-②) occurred even if pre-dilation was successful and stent surgery was required, the subject was excluded from screening. And alternative treatments are implemented according to the institution's standard procedures. 6. After pre-dilation is successful, 1) In case of large vessel (diameter 3.0 mm or more), measure the myocardial fractional flow reserve (FFR) and if the FFR measurement value is > 0.8, register for this clinical trial. ☞ *If the FFR measurement value is ≤ 0.8, the patient will be excluded*

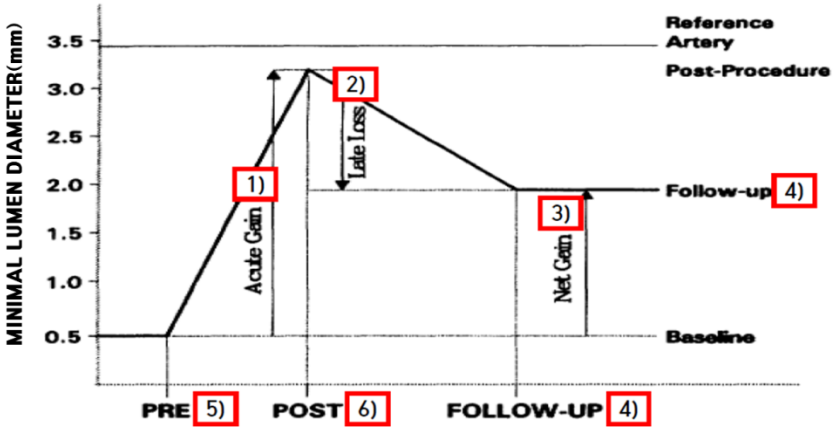
from screening and alternative treatment (DES (Drug elution stent) insertion, etc.) will be performed according to institutional procedures.
2) In case of small vessels (over 2.0 mm in diameter but less than 3.0 mm), register for this clinical trial without measuring FFR.
※ If there are two or more lesions that meet the inclusion criteria, the lesion with the narrowest minimum lumen diameter is selected as the target lesion.

7. investigational devices are applied only to subjects who meet the selection and exclusion criteria. After applying investigational device, the procedure is terminated when observation and testing for adverse events and effectiveness evaluation are completed. At this time, the method of applying investigational devices is as follows.

<How to apply medical devices for clinical trial>
Minimize the time from when the DCB contacts the blood vessel until it expands to the nominal pressure to within 3 minutes. If 3 minutes are exceeded, remove the failed DCB, replace it with a new product, and perform the procedure again. The drug-coated balloon catheter should be 2-3 mm longer on the side than the pre-dilated standard balloon, and the balloon diameter should match the reference vessel diameter. (for details, refer to 8.3. Instructions for use and precautions for use of investigational devices)

8. After the procedure is completed, the subject continues to be hospitalized for observation, and the time of discharge is determined by the investigator according to the institution's standard procedures.
9. Subjects will visit at 1 and 6 months after the procedures to check effectiveness and safety.
10. At 6 months after the procedures, coronary angiography was performed and the coronary angiography images are stored for effectiveness evaluation.
11. During the follow-up period, if stenosis of more than 50% in the target lesion, angina pectoris or myocardial ischemia is suspected, revascularization(ischemia-driven target lesion revascularization(ID-TLR) or Target Vessel Revascularization(TVR)) is performed.
    ☞ *Subjects who have undergone revascularization of target lesions visit on unscheduled visit days for examination and observation.*
12. After completing the follow-up evaluation at 6 months after the procedure, if no adverse events have occurred or if all adverse events that have already occurred are resolved, the subject's clinical trial visit is terminated. However, if the investigator determines that follow-up is no longer necessary for a subject whose adverse event has not been completely resolved, the subject's visit may be terminated 6 months after the procedure.

	☞ *If there are adverse events or residual symptoms due to adverse events even after the end of the clinical trial, medical measures are taken according to the institution's standard medical guidelines.* ※ *If concomitant therapy is administered during the clinical trial, it must be recorded in the case report form.* ※ *Coronary angiography images taken during the procedure and follow-up period are collectively delivered to the evaluator for effectiveness evaluation.*
Effectiveness evaluation variable	<Primary efficacy endpoint> ■ In-lesion late lumen loss (mm) at 6 months after the procedure <Secondary efficacy endpoint> ■ Device success rate(N%) ■ Procedural success rate(N%) ■ Restenosis rate(%) at 6 months after the procedure ■ Target vessel failure(TVF) incidence rate(%) at 6 months after the procedure
Effectiveness evaluation criteria and methods	<Primary efficacy endpoint> ■ In-lesion late lumen loss (mm) at 6 months after the procedure Late luminal loss within the lesion is evaluated on coronary angiography imaging at 6 months after the procedure. ① Definition of In-lesion In-lesion is defined as the section corresponding to both ends of the lesion. ② Definition of Late lumen loss (LLL, ㎜) LLL(mm) is defined as the value obtained by subtracting the changed vessel diameter(MLD, mm) after the follow-up period(6 months) from the dilated vessel diameter(MLD, mm) immediately after vascular intervention. Vessel diameter refers to the diameter measured based on the narrowest section within the lesion (see figure).



- Late loss(㎜) (2) = Acute gain(㎜) (1) - Net Gain(㎜) (3)
- Acute gain(㎜) (1) = Post-procedure MLD(㎜) (6) - Pre-procedure MLD(㎜) (5)
- Net gain(㎜) (3) = Follow-up MLD(㎜) (4) - Pre-procedure MLD(㎜) (5)

Figure. Definition of Late lumen loss (LLL)

Late Lumen Loss (㎜), Richard E. Kuntz et al., 1992, ISSN: 1524-4539

<Secondary efficacy endpoint>

■ Device success rate (N%)

During the procedure, when the distal part of the clinical trial medical device successfully reaches the target lesion and the balloon operates normally inflated and deflated and is recovered intact without rupture, the device is defined as successful, and the device success rate is evaluated.

■ Procedural success rate (N%)

In addition to success on coronary angiography[1)], it is defined as the absence of TLF (cardiac death, myocardial infarction attributable to target vessel (TV-MI), or ID-TLR) during hospitalization, and the success rate of the procedure is evaluated.

[1)] It is defined as a case where residual stenosis is less than 30% immediately after the treatment of the target lesion, blood flow is normal, and vascular dissection is confirmed to a degree that does not impede blood flow. At this time, residual stenosis is evaluated through coronary angiography images.

■ Restenosis rate (%) at 6 month after procedure

When a successfully treated lesion is evaluated through coronary angiography, restenosis is defined as a diameter stenosis(DS)** compared to the reference vessel diameter of 50% or more, and is evaluated at 6 months after the procedure. At this time, stenosis rate(DS,%) is evaluated through coronary angiography images.

	** Definition of stenosis rate(DS, %) = (1-[MLD/RVD]) X 100 ① Definition of in-lesion MLD(minimal lumen diameter, mm) It is defined as the diameter of the narrowest blood vessel measured through coronary angiography. ② RVD (Reference vessel diameter, mm) It is defined as the average obtained by measuring the distal and proximal diameters of a certain section of the normal part of the blood vessel with the target lesion. ■ Target vessel failure(TVF) incidence rate (%) at 6 months after the procedure TVF evaluates incidence rates. TVF Definition: Composite of Cardiac Death, TV-MI, or ID-TVR
Safety evaluation variable	■ Adverse events ■ MACE(Major Adverse Cardiac Event) at 6 months after the procedure
Safety evaluation criteria and methods	■ Adverse events In this clinical trial, adverse events are classified into adverse events that occurred before the application of the investigational device and adverse events that occurred after the application of the clinical trial medical device (Treatment Emergent Adverse Event, TEAE). (The definition and evaluation of adverse events is referred to '15. Evaluation criteria, evaluation methods, and reporting methods for safety, including side effects' section.) Adverse events that occurred before application of medical devices for clinical trials are recorded as adverse events before treatment, but are excluded from adverse event analysis. In other words, adverse event analysis targets TEAEs. All adverse events that occur are standardized into SOC (System Organ Class) and PT (Preferred Term) using the latest version of MedDRA (Medical Dictionary for Regulatory Activities). ■ MACE(Major Adverse Cardiac Event) 6 months after the procedure ① Cardiac death : Death of unknown cause is classified as cardiac, and according to the definition of ARC, Composite endpoint of cardiac death (CEC) indicates the possibility of restenosis of the target lesion, and death accompanied by thrombosis of the target lesion is determined to be the cause of cardiac death.

	② Whether myocardial infarction(MI) occurred or not : It is evaluated as ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction. ST-segment elevation myocardial infarction: When there is persistent chest pain for more than 30 minutes, the CK-MB fraction increases to more than three times the normal level, and the ST segment is elevated on an electrocardiogram. Non-ST-segment elevation myocardial infarction: When the ST segment is not elevated on an electrocardiogram. ③ Whether Target vessel Thrombosis occurred or not : According to the definition of ARC, it is classified and evaluated as follows. • Certainty of diagnosis: definite/probable/possible • Elapsed time: Early (0-30 days)/Late (31-180 days) from interventional surgery ④ Whether revascularization is performed: ID-TLR, TVR - ID-TLR(Ischemia-Driven Target Lesion Revascularization) is a percutaneous intervention for the target lesion if the treated target lesion has an internal diameter stenosis of more than 50% and symptoms of angina pectoris, myocardial ischemia is suspected in an objective test, or both exist. Defined as one case - TVR (Target Vessel Revascularization) is defined as any percutaneous intervention or coronary artery bypass surgery performed on the treated target vessel.
Observation items	[refer to clinical trial schedule]
Predicted adverse events	The following adverse events may occur, and signs, symptoms, or diseases other than those listed may also occur. <Adverse cases related to coronary intervention surgery> • Acute myocadiac infarction • Allergic reaction • Aneurysm or Pseudoaneurysm • Rupture of coronary artery • Hematoma • Bleeding / bleeding requiring blood transfusion • Low blood pressure / high blood pressure

	• Arrythmia including ventricular fibrillation(VF), ventricular tachycardia(VT) • Cardiac tamponade or Pericardial effusion • Cardiogenic shock / Pulmonary edema • coronary artery spasm(CAS) • Death • fever • Heart failure • Localized or systemic infection • Inflammation • Vascular occlusion • Pain or tenderness at access site • Renal failure • Stroke, cerebrovascular disorder/ transient ischemic attack(TIA) • Systemic embolic occlusion • Thrombosis <Adverse cases related to Drug(paclitaxel)> • Allergy / immune response • Alopecia • Anemia • Blood transfusion • Digestive system symptoms • Blood diseases(leukopenia, neutropenia, thrombocytopenia) • Alterations in liver enzymes • Alterations in blood vessel wall tissue, including infection, cell damage, or necrosis. • Muscle pain/joint pain • Peripheral neuropathy • Cardiac conduction abnormalities • Pseudomembranous colitis

[CLINICAL TRIAL PROGRESS SCHEDULE]

	Screening	Procedure day	Follow-up period		Unscheduled visit##
Visit	**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**-**
Elapsed days	**- 4w ~ 0day§**	**0day§**	**1M after procedure**	**6M after procedure**	**-**
Visit Window	**-**	**-**	**± 2w**	**± 1M**	**-**
Observation type	**Visit/Adm**	**Adm/Visit**	**Visit**	**Visit**	**Adm/Visit**
Obtain written consent[1)]	√				
Selection/Exclusion Criteria	√	√			
Demographic survey[2)]	√				√
Medical history/surgery/procedure history[3)]	√				
Preceding medication[4)]	√				

Physical examination[5)]		√	√§§§			√
Vital signs[6)]		√	√§§§	√	√	√
Pregnancy test[7)]		√				√
Laboratory tests[8)]	General blood tests	√§§		√	√	√
	Serum biochemical test	√§§		√	√	√
	Myocardial enzyme test*	√§§	√			
	blood coagulation test	√§§				
	Glycated hemoglobin test**	√§§			√	√
	urine test	√§§				
Electrocardiogram[9)]		√§§§§	√**	√	√	√
Echocardiography[10)]		√				
Coronary angiography[11)]			√		√	√
PCI (Percutaneous Coronary Intervention) [12)]	Pre dilation		√			
	FFR measurements		(√)[b]			
	Application of investigational device		√			
revascularization[13)]						√
Check whether the device was successful[14)]			√			
Check whether the procedure was successful[15)]			√#			
Check for MACE[16)]			√	√	√	√
Adverse events/serious adverse events[17)]			√	√	√	√
concomitant therapy[18)]			√	√	√	√

[DEFINITION OF ABBREVIATIONS AND TERMS]

[Abbreviation]

약어	의미
aPTT	activated Partial thromboplastin time
API	Active pharmaceutical ingredient
ADE	Adverse Device Effect
AE	Adverse Event
ALT	Alanine aminotransferase
ALP	Alkaline phosphatase
AST	Aspartate aminotransferase

BUN	Blood urea nitrogen
CRA	Clinical Research Associate
CS	Clinically Significant
DS	Diameter stenosis
FA set	Full Analysis Set
Hct	Hematocrit
Hb	Hemoglobin
IRB	Institutional Review Board
ICH-GCP	International Conference on Harmonization-Good Clinical Practice
KGCP	Korea Good Clinical Practice
LOCF	Last Observation Carried Forward
LPO	Last Patient Out
LLL	Late lumen loss
MACE	Major adverse cardiovascular event
MLD	Minimum lumen diameter
NCS	Not Clinically Significant
POBA	plain old balloon angioplasty,
PP set	Per Protocol Set
PT	Preferred Term
RBC	Red blood cell
RVD	Reference vessel diameter
SAE	Serious Adverse Event
SOC	System Organ Class
TLF	Target lesion failure
TVF	Target vessel failure
TLR	Target lesion revascularization
TVR	Target vessel revascularization
TEAE	Treatment Emergent Adverse Event

[Terms]

용어	의미
De novo lesion	Coronary artery lesion that has never been treated with any interventional procedure (e.g., balloon angioplasty, stent, rotational atherectomy, laser treatment, etc.)
In-lesion	Sections corresponding to both ends of the lesion
Late lumen loss(LLL)	The value obtained by subtracting the change in vessel diameter (MLD, mm) after the follow-up period (6 months) from the dilated vessel diameter (MLD, mm) immediately after vascular intervention.
DS(Diameter stenosis)	Definition of diameter stenosis relative to reference vessel (DS, %) = (1-[MLD/RVD]) X 100
MLD(Minimal lumen diameter)	Diameter of the narrowest blood vessel as measured by coronary angiography
RVD(Reference vessel diameter)	Average obtained by measuring the distal and proximal diameters of a certain section of the normal part of the blood vessel with the target lesion
TLF(Target lesion failure)	Cardiac death, target vessel myocardial infarction (TV-MI), or ischemia-driven target lesion revascularization(ID-TLR)
TVF(Target vessel failure)	Cardiac death, target vessel myocardial infarction (TV-MI), or ischemia-driven target vessel revascularization (ID-TVR)
ID-TLR(ischemia-driven Target Lesion Revascularization)	Percutaneous intervention was performed on the target lesion when the treated target lesion had an internal diameter stenosis of more than 50% and symptoms of angina pectoris, myocardial ischemia was suspected in an objective test, or both were present.
TVR(Target Vessel Revascularization)	If any percutaneous intervention or coronary artery bypass surgery was performed on the treated target blood vessel
AE(Adverse Event)	Any unintended signs (including abnormalities in laboratory test results, etc.), symptoms, or diseases that occur in subjects during clinical trials
ADE(Adverse Device Effect)	Any harmful and unintended reactions caused by investigational medical devices
Unexpected Adverse Device Effect	Differences in the pattern of adverse device effects or degree of harm in light of available medical device-related information, such as the clinical investigator data sheet or medical device attachment documents.

1. TITLE OF CLINICAL TRIAL

A Small scale, Prospective, Multicenter, Single arm, Investigator-Initiated Feasibility Clinical Study to Evaluate the Efficacy and Safety of Paclitaxel Coated PTCA Balloon Catheter (GENOSS® DCB) in Patients with De novo lesion of coronary artery

2. NAME AND LOCATION OF CLINICAL TRIAL INSTITUTION

■ Hallym University Kangnam Sacred Heart Hospital
(07441) 1 Singil-ro, Yeongdeungpo-gu, Seoul (Daerim-dong 948-1)
Main phone: 1577-5587

■ Severance Hospital
(03722) 50-1 Yonsei-ro, Seodaemun-gu, Seoul
Main phone: 1594-1004

3. NAME AND TITLE OF CLINICAL TRIAL PRINCIPAL INVESTIGATOR, SUB-INVESTIGATOR, AND CO-RESEARCHER

■ Name and title of coordinating investigator and principal investigator

Clinical trial institution	Name and title	department	e-mail	contact
Hallym University Kangnam Sacred Heart Hospital	Prof. Jung Rae Cho	Cardiology	jrjoe@naver.com	02-829-5109
Severance Hospital	Prof. Jung Sun Kim	Cardiology	KJS1218@yuhs.ac	02-2288-8457

■ Name and title of sub-investigator and co-researcher

▷ Refer to 'Appendix B_ Investigators and Clinical Trial Support Organization'

4. NAME AND TITLE OF INVESTIGATIONAL DEVICES MANAGER

▷ Refer to 'Appendix B_ Investigators and Clinical Trial Support Organization'

5. NAME AND ADDRESS OF INVESTIGATOR

Hallym University Kangnam Sacred Heart Hospital
(07441) 1 Singil-ro, Yeongdeungpo-gu, Seoul (Daerim-dong 948-1)

6. PURPOSE AND BACKGROUND OF CLINICAL TRIAL

6.1. Background

Percutaneous coronary intervention(PCI), a representative treatment method for coronary artery disease(CAD) that causes angina, myocardial infarction, asymptomatic myocardial ischemia, and sudden death due to acute cardiac arrest, has developed rapidly over the past 30 years.[1,2] However, acute complications such as subintimal dissection, stenosis, and abrupt vessel closure due to mechanical damage that occurs as the balloon expands, and problems related to restenosis, which occurs in 30 to 60% of cases within 6 months after the procedure, are still continuously raised[3]. With the advent of stents in the mid-1980s, it was confirmed that they reduced the elastic recoil of coronary arteries and restenosis caused by late negative vessel remodeling, which were fatal disadvantages of balloon angioplasty, and thus significantly reduced repeat revascularization, thereby reducing the risk of coronary artery disease. Although it has become one of the major standard treatments for cancer, it has caused new incurable conditions such as late stent thrombosis and in-stent restenosis[4]. Afterwards, antithrombotic drug therapy using antiplatelet agents(Aspirin+Ticlopidine or Clopidogrel) was developed, and the incidence of stent thrombosis decreased. However, to reduce ISR, drugs(sirolimus, paclitaxel, etc.) that inhibit the proliferation of neointima after stent insertion have been attempted, and drug-eluting stents(DES) have been developed as a method to apply the drugs locally only to lesions to reduce the systemic side effects of these drugs. However, even in the case of drug-eluting stents, it is not easy to always maintain a constant release concentration of the drug, and new problems have arisen[4], such as the concerns of stent thrombosis[5] and the increased risk of hemorrhagic side effects following long-term administration[6] of dual antiplatelet drugs.

Drug-coated balloon catheters(DCB) have emerged as a new concept for the treatment of coronary artery disease(CAD) and are an established treatment option for in-stent restenosis of bare metal stent (BMS) and DES. This technology is based on rapid delivery of a highly lipophilic drug to the blood vessel wall after balloon inflation.[7, 8] This technology is based on rapid delivery of a highly lipophilic drug to the blood vessel wall after balloon inflation[6]. The effectiveness and safety of DCB in de novo small vessel disease(SVD) have been demonstrated in a recent large study, which showed similar MACE rates after 12 months in patients treated with DCB or second-generation DES[9]. CAD treatment using drug-coated balloon catheters(DCB) benefits from localized drug delivery and a 'leave nothing behind' strategy. The principle of using DCB in the treatment of intracoronary de novo lesions is based on the concept that for lipophilic drugs, a short contact time between the balloon surface and the vessel wall is sufficient for effective drug delivery[10]. Many clinical studies have been

conducted under this concept and have proven that DCB is safe and effective for specific indications.

Various DCB studies targeting new lesions have been conducted. In Kleber's study, when paclitaxel-coated DCB was used on 58 patients with new lesions, 69% of patients showed positive remodeling(Compensatory dilatation of the artery to maintain its inner diameter despite increasing lesion volume). At the same time, 29% of patients reported mild luminal loss[11]. In another study, DCB was applied to 45 new lesions, 22 of which were treated with stents, and the two groups were compared. In the group where only DCB was applied, the value of LLL was significantly smaller, confirming its effectiveness in vasodilation[12]. In Nishiyama[13]'s study, the MLD of the group that applied DCB and the group that applied DES were compared, and the MLD value was significantly larger in the group that applied DCB, confirming that the treatment effect was better than DES. These results show that the value of DCB is promising not only in patients with coronary ISR(In-stent Restenosis) but also in de novo lesions[11]. In addition, several other studies have shown that paclitaxel is rapidly absorbed into vascular smooth muscle cells within blood vessels, and that the anti-proliferation effect lasts for about 2 weeks even with short-term exposure, and has an inhibitory effect on cell proliferation and prevention of restenosis compared to long-term exposure. It has been proven that they are almost identical in terms of persistence[4]. Treatment of CAD using DCB has the advantage of ensuring uniform distribution of the drug, preventing stent thrombosis because it does not leave a stent, and shortening the administration of antiplatelet drugs[14].

According to the third report of the international DCB consensus group, drug-coated balloons(DCBs) are a promising treatment for coronary artery disease based on rapid and uniform delivery of antiproliferative drugs to the vessel wall during a single balloon inflation using a lipophilic matrix without the use of a permanent implant. And potentially all Percutaneous coronary interventions(PCI) should aim to use a DCB-only strategy, meaning a similar approach for all lesion preparations. This requires optimal angioplasty outcomes, which can be assessed using angiography, physiology or intravascular imaging, and drug delivery is performed with DCB.[15]

Under this background, Genoss Co., Ltd. developed Genoss® DCB, Paclitaxel Coated PTCA Balloon Catheter, and conducted clinical trials on people with Coronary ISR from November 2016 to February 2019. The primary efficacy evaluation was in-segment late lumen loss in coronary angiography performed 6 months after DCB application, which was 0.15 ± 0.43 mm in the Genoss® DCB group and 0.24 ± 0.39 mm in the Sequent® Please DCB, compared to conventional DCB. It was approved by the Ministry of Food and Drug Safety after proving that it is not inferior[16]. In this clinical trial, we aim to confirm clinical feasibility through a small-scale, single-group, investigator-initiated pilot study targeting people with de novo lesions.

6.2. Purpose of clinical trial

Genoss® DCB, Paclitaxel Coated PTCA Balloon Catheter, has received approval from the Ministry of Food and Drug Safety for in-stent restenosis(ISR), but has not been evaluated for new lesions.

Therefore, this study aims to evaluate the clinical feasibility through a small-scale, multicenter, single-group, investigator-initiated pilot study targeting patients with de novo lesions measuring 2.0 mm to 4.0 mm in diameter.

7. INVESTIGATIONAL DEVICES

7.1. Overview of investigational devices

■ Overview of the test device (GENOSS® DCB)

1) Overview

An Overview of the test device is shown in the table below.

Table 1. Overview of test device

Item	Detail
Common name	Drug-Coated PTCA Balloon Catheter
Classification number [class]	A57130.21 [class 4]
Certificate number	Certificate no. 20-501 (Approved for use in the treatment of in-stent restenosis)
Product name	GENOSS® DCB
Manufacturer	Genoss Co., Ltd
Transportation/Storage method	Store at room temperature (1℃ ~ 30℃) in a dry and dark place.

2) Appearance

A. Exterior photo

1 Full photo

a. Full photo of the product

b. Packaging photo

<1st Tyvek Pouch packaging>

<2nd Aluminum Foil Pouch packaging>

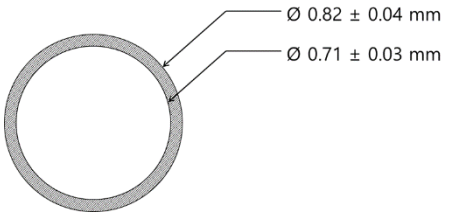
2 Balloons

a. Before expansion

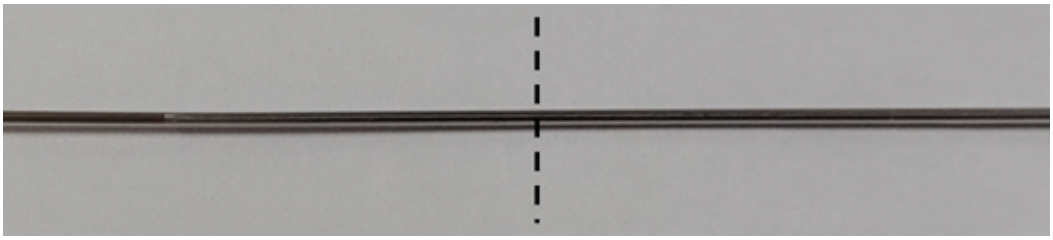
b. After expansion

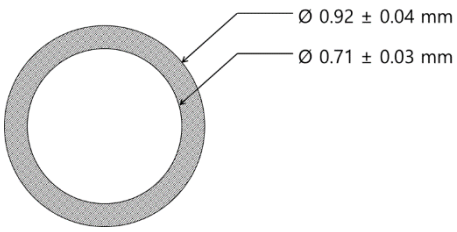
3 Body

a. Distal shaft (anterior part)

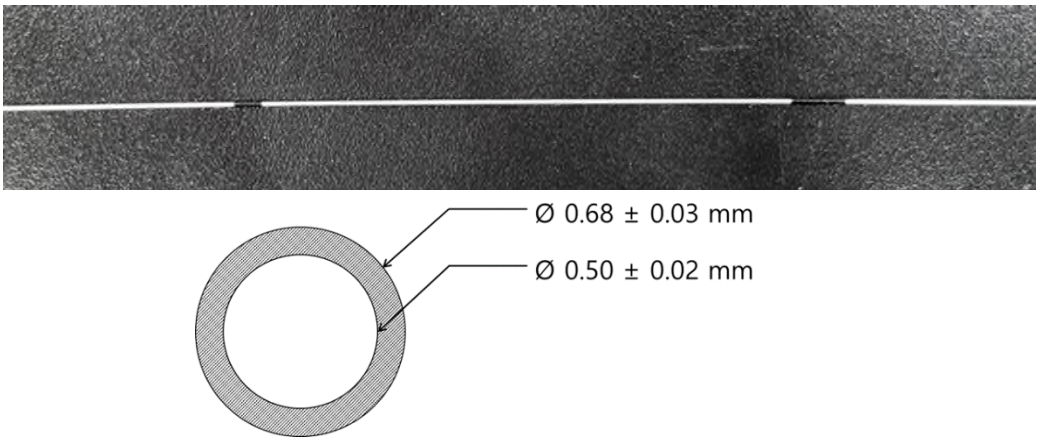


b. Distal shaft (posterior part)

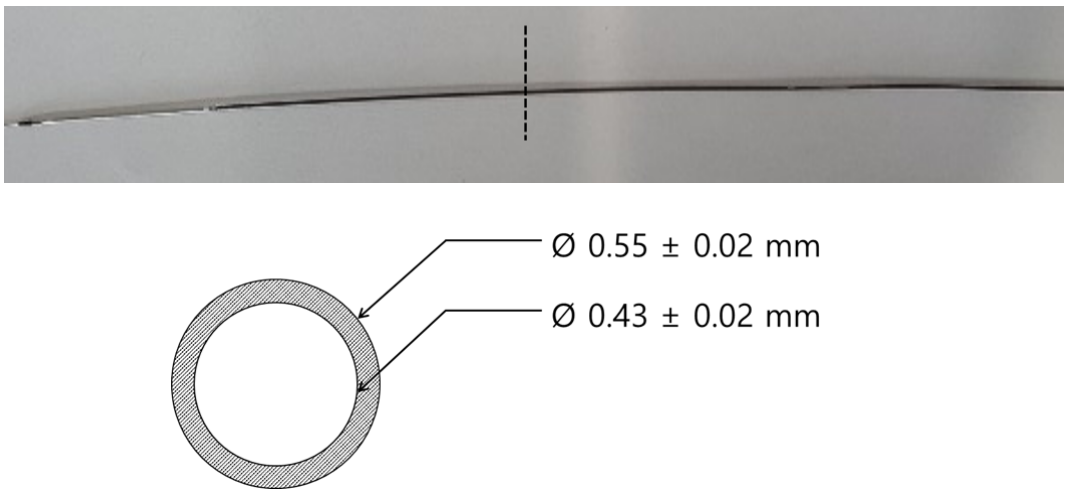




c. Proximal shaft



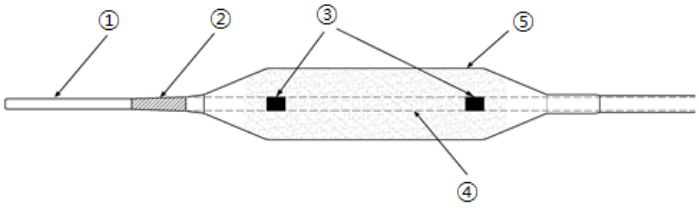
d. Guide wire tube



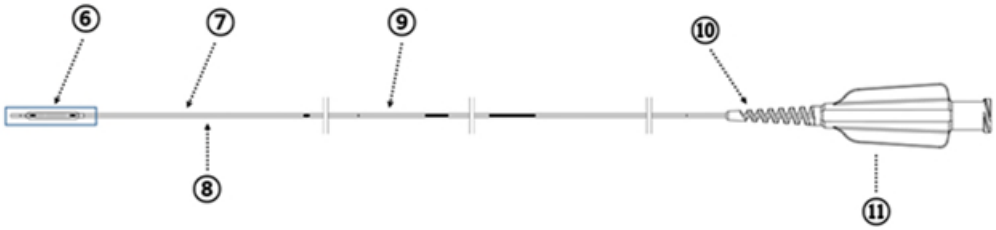
4 Hub

B. Appearance description

1 Structure of balloon

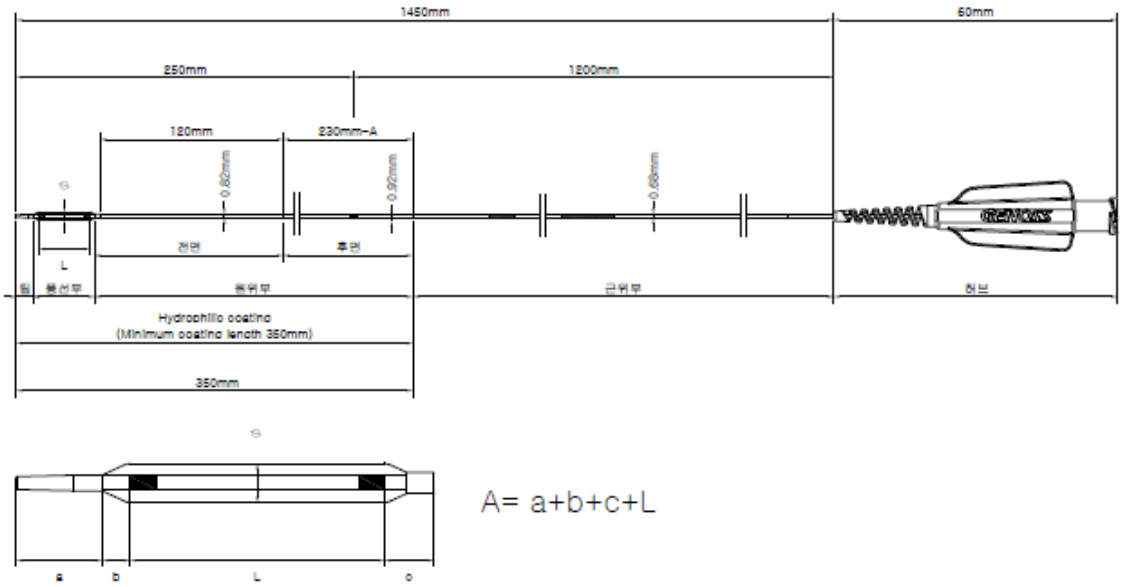


2 Overall structure



번호	명 칭	설 명
①	Storage mandrel	Maintains the shape of Distal shaft
②	End tip	A part that facilitates advancement of the catheter through the stricture to be dilated and smooth movement of the balloon from the guide wire.
③	Radiopaque marker	The position of the balloon catheter can be checked during radiation irradiation, and there are two markers.
④	Guidewire tube	The part where the guide wire passes
⑤	Drug coated balloon	Paclitaxel drug is coated on the surface of the balloon, so when the balloon is inflated, it comes into contact with the lesion on the blood vessel wall and is the part where the antiproliferative drug is delivered.
⑥	Protector tube	Balloon part and drug coating protective tube
⑦	Distal shaft	Tube located at the distal end of the balloon contributes to balloon inflation.
⑧	Hydrophilic coating	Surface coating on the balloon and distal shaft to facilitate lesion entry
⑨	Proximal shaft	Main body parts of balloon catheter
⑩	Strain relief	A connection located between the shaft and hub to reduce the burden caused by pressure.
⑪	Hub	Port connecting the proximal end of the catheter to an inflation device

3) Size



A= a+b+c+L

L : Distance of marker (Balloon length)

Model name	Balloon					Shaft			Valid length (mm)
	Balloon length (mm)	Outer diameter of expanded balloon (mm)	Distance of marker (mm)	Balloon surface area (mm^2)	Nominal pressure (atm)	Distal anterior diameter (mm)	Distal posterior diameter (mm)	Proximal diameter (mm)	
GDEB-10-200	10	2.01	10	62.80	8	0.82	0.92	0.68	1450
GDEB-10-225	10	2.25	10	70.65	8	0.82	0.92	0.68	1450
GDEB-10-250	10	2.50	10	78.50	8	0.82	0.92	0.68	1450
GDEB-10-275	10	2.75	10	86.35	8	0.82	0.92	0.68	1450
GDEB-10-300	10	3.00	10	94.20	8	0.82	0.92	0.68	1450
GDEB-10-325	10	3.25	10	102.05	8	0.82	0.92	0.68	1450
GDEB-10-350	10	3.50	10	109.90	8	0.82	0.92	0.68	1450
GDEB-10-375	10	3.73	10	117.75	8	0.82	0.92	0.68	1450
GDEB-10-400	10	4.00	10	125.60	8	0.82	0.92	0.68	1450
GDEB-15-200	15	2.01	15	94.20	8	0.82	0.92	0.68	1450
GDEB-15-225	15	2.25	15	105.98	8	0.82	0.92	0.68	1450
GDEB-15-250	15	2.50	15	117.75	8	0.82	0.92	0.68	1450
GDEB-15-275	15	2.75	15	129.53	8	0.82	0.92	0.68	1450
GDEB-15-300	15	3.00	15	141.30	8	0.82	0.92	0.68	1450
GDEB-15-325	15	3.25	15	153.08	8	0.82	0.92	0.68	1450
GDEB-15-350	15	3.50	15	164.85	8	0.82	0.92	0.68	1450

GDEB-15-375	15	3.73	15	176.63	8	0.82	0.92	0.68	1450
GDEB-15-400	15	4.00	15	188.40	8	0.82	0.92	0.68	1450
GDEB-18-200	18	2.01	18	113.04	8	0.82	0.92	0.68	1450
GDEB-18-225	18	2.25	18	127.17	8	0.82	0.92	0.68	1450
GDEB-18-250	18	2.50	18	141.30	8	0.82	0.92	0.68	1450
GDEB-18-275	18	2.75	18	155.43	8	0.82	0.92	0.68	1450
GDEB-18-300	18	3.00	18	169.56	8	0.82	0.92	0.68	1450
GDEB-18-325	18	3.25	18	183.69	8	0.82	0.92	0.68	1450
GDEB-18-350	18	3.50	18	197.82	8	0.82	0.92	0.68	1450
GDEB-18-375	18	3.73	18	211.95	8	0.82	0.92	0.68	1450
GDEB-18-400	18	4.00	18	226.08	8	0.82	0.92	0.68	1450
GDEB-20-200	20	2.01	20	125.60	8	0.82	0.92	0.68	1450
GDEB-20-225	20	2.25	20	141.30	8	0.82	0.92	0.68	1450
GDEB-20-250	20	2.50	20	157.00	8	0.82	0.92	0.68	1450
GDEB-20-275	20	2.75	20	172.70	8	0.82	0.92	0.68	1450
GDEB-20-300	20	3.00	20	188.40	8	0.82	0.92	0.68	1450
GDEB-20-325	20	3.25	20	204.10	8	0.82	0.92	0.68	1450
GDEB-20-350	20	3.50	20	219.80	8	0.82	0.92	0.68	1450
GDEB-20-375	20	3.73	20	235.50	8	0.82	0.92	0.68	1450
GDEB-20-400	20	4.00	20	251.20	8	0.82	0.92	0.68	1450
GDEB-23-200	23	2.01	23	144.44	8	0.82	0.92	0.68	1450
GDEB-23-225	23	2.25	23	162.50	8	0.82	0.92	0.68	1450
GDEB-23-250	23	2.50	23	180.55	8	0.82	0.92	0.68	1450
GDEB-23-275	23	2.75	23	198.61	8	0.82	0.92	0.68	1450
GDEB-23-300	23	3.00	23	216.66	8	0.82	0.92	0.68	1450
GDEB-23-325	23	3.25	23	234.72	8	0.82	0.92	0.68	1450
GDEB-23-350	23	3.50	23	252.77	8	0.82	0.92	0.68	1450
GDEB-23-375	23	3.73	23	270.83	8	0.82	0.92	0.68	1450
GDEB-23-400	23	4.00	23	288.88	8	0.82	0.92	0.68	1450
GDEB-25-200	25	2.01	25	157.00	8	0.82	0.92	0.68	1450
GDEB-25-225	25	2.25	25	176.63	8	0.82	0.92	0.68	1450
GDEB-25-250	25	2.50	25	196.25	8	0.82	0.92	0.68	1450
GDEB-25-275	25	2.75	25	215.88	8	0.82	0.92	0.68	1450
GDEB-25-300	25	3.00	25	235.50	8	0.82	0.92	0.68	1450
GDEB-25-325	25	3.25	25	255.13	8	0.82	0.92	0.68	1450
GDEB-25-350	25	3.50	25	274.75	8	0.82	0.92	0.68	1450
GDEB-25-375	25	3.73	25	294.38	8	0.82	0.92	0.68	1450
GDEB-25-400	25	4.00	25	314.00	8	0.82	0.92	0.68	1450

GDEB-30-200	30	2.01	30	188.40	8	0.82	0.92	0.68	1450
GDEB-30-225	30	2.25	30	211.95	8	0.82	0.92	0.68	1450
GDEB-30-250	30	2.50	30	235.50	8	0.82	0.92	0.68	1450
GDEB-30-275	30	2.75	30	259.05	8	0.82	0.92	0.68	1450
GDEB-30-300	30	3.00	30	282.60	8	0.82	0.92	0.68	1450
GDEB-30-325	30	3.25	30	306.15	8	0.82	0.92	0.68	1450
GDEB-30-350	30	3.50	30	329.70	8	0.82	0.92	0.68	1450
GDEB-30-375	30	3.73	30	353.25	8	0.82	0.92	0.68	1450
GDEB-30-400	30	4.00	30	376.80	8	0.82	0.92	0.68	1450
GDEB-35-200	35	2.01	35	219.80	8	0.82	0.92	0.68	1450
GDEB-35-225	35	2.25	35	247.28	8	0.82	0.92	0.68	1450
GDEB-35-250	35	2.50	35	274.75	8	0.82	0.92	0.68	1450
GDEB-35-275	35	2.75	35	302.23	8	0.82	0.92	0.68	1450
GDEB-35-300	35	3.00	35	329.70	8	0.82	0.92	0.68	1450
GDEB-35-325	35	3.25	35	357.18	8	0.82	0.92	0.68	1450
GDEB-35-350	35	3.50	35	384.65	8	0.82	0.92	0.68	1450
GDEB-35-375	35	3.73	35	412.13	8	0.82	0.92	0.68	1450
GDEB-35-400	35	4.00	35	439.60	8	0.82	0.92	0.68	1450
GDEB-40-200	40	2.01	40	251.20	8	0.82	0.92	0.68	1450
GDEB-40-225	40	2.25	40	282.60	8	0.82	0.92	0.68	1450
GDEB-40-250	40	2.50	40	314.00	8	0.82	0.92	0.68	1450
GDEB-40-275	40	2.75	40	345.40	8	0.82	0.92	0.68	1450
GDEB-40-300	40	3.00	40	376.80	8	0.82	0.92	0.68	1450
GDEB-40-325	40	3.25	40	408.20	8	0.82	0.92	0.68	1450
GDEB-40-350	40	3.50	40	439.60	8	0.82	0.92	0.68	1450
GDEB-40-375	40	3.73	40	471.00	8	0.82	0.92	0.68	1450
GDEB-40-400	40	4.00	40	502.40	8	0.82	0.92	0.68	1450

4) Principle of operation

This product is a balloon-expandable catheter used during percutaneous coronary angioplasty (PTCA). When the balloon is inflated in an area where problems such as vascular stenosis or occlusion occur, the pressure of the balloon's inflation causes pressure on the stenosis or foreign substances such as plaque on the blood vessel wall. This causes the narrowed blood vessels to widen. At this time, the antiproliferative Paclitaxel drug coated on the surface of the balloon comes into contact with the blood vessel wall and penetrates the target tissue, thereby reducing and preventing restenosis within the stent due to new lesions or late lumen loss of the stent. This product allows easy balloon placement through a radiopaque marker band used in fluoroscopic examination, and the catheter has a tapered tip, allowing easy insertion into the stenosis area through a guidewire.

5) Product characteristics

Balloon diameter (mm)	2.01, 2.25, 2.50, 2.75, 3.00, 3.25, 3.50, 3.73, 4.00, ±10%
Balloon length (mm)	10, 15, 18, 20, 23, 25, 30, 35, 40, ±5%
Catheter valid length (cm)	145 ±7.25
Nominal pressure of inflation (NP)	8atm
Rated burst pressure (RBP)	16atm (2mm ~ 3.5mm), 14atm (3.75mm, 4.00mm)
Balloon deflation time	< 15 seconds
Guide wire diameter	≤ 0.014" (0.356mm)
Catheter proximal outer diameter (mm)	0.68 ± 0.03
Catheter distal outer diameter (mm)	Anterior : 0.82 ±0.04 / Posterior : 0.92 ±0.04
Crossing profile (mm)	0.92 ± 0.04

6) Performance

1. IN VITRO BALLOON COMPLIANCE INFORMATION

(atm)	(MPa)	Balloon inflated diameter (mm)								
8 (NP)	0.81	2.01	2.25	2.50	2.75	3.00	3.25	3.50	3.73	4.00
9	0.91	2.04	2.27	2.52	2.77	3.04	3.30	3.55	3.76	4.02
10	1.01	2.06	2.29	2.55	2.80	3.07	3.34	3.60	3.79	4.05
11	1.11	2.08	2.31	2.57	2.82	3.10	3.37	3.64	3.82	4.08
12	1.22	2.11	2.34	2.60	2.85	3.14	3.41	3.68	3.86	4.11
13	1.32	2.14	2.36	2.63	2.87	3.17	3.44	3.72	3.89	4.14
14	1.42	2.17	2.38	2.66	2.89	3.20	3.48	3.76	3.92	4.17
15	1.52	2.19	2.40	2.69	2.92	3.24	3.51	3.79	3.95	4.20
16 (RBP)	1.62	2.22	2.43	2.72	2.95	3.28	3.56	3.84	3.97	4.24
17	1.72	2.25	2.46	2.75	2.99	3.31	3.59	3.88	4.01	4.27
18	1.82	2.29	2.49	2.79	3.02	3.34	3.63	3.93	4.04	4.30

NP (Nominal pressure) RBP (Rate Burst Pressure)

2. BALLOON DRUG AMOUNT INFORMATION

Model	Length (mm)	Diameter (mm)	Balloon surface area (mm^2)	Drug content per unit area ($\mu g/mm^2$)	Drug content (μg)
GDEB-10-200	10	2	62.80	3	188.40
GDEB-10-225	10	2.25	70.65	3	211.95
GDEB-10-250	10	2.5	78.50	3	235.50
GDEB-10-275	10	2.75	86.35	3	259.05
GDEB-10-300	10	3	94.20	3	282.60
GDEB-10-325	10	3.25	102.05	3	306.15
GDEB-10-350	10	3.5	109.90	3	329.70
GDEB-10-375	10	3.75	117.75	3	353.25
GDEB-10-400	10	4	125.60	3	376.80
GDEB-15-200	15	2	94.20	3	282.60
GDEB-15-225	15	2.25	105.98	3	317.93

GDEB-15-250	15	2.5	117.75	3	353.25
GDEB-15-275	15	2.75	129.53	3	388.58
GDEB-15-300	15	3	141.30	3	423.90
GDEB-15-325	15	3.25	153.08	3	459.23
GDEB-15-350	15	3.5	164.85	3	494.55
GDEB-15-375	15	3.75	176.63	3	529.88
GDEB-15-400	15	4	188.40	3	565.20
GDEB-18-200	18	2	113.04	3	339.12
GDEB-18-225	18	2.25	127.17	3	381.51
GDEB-18-250	18	2.5	141.30	3	423.90
GDEB-18-275	18	2.75	155.43	3	466.29
GDEB-18-300	18	3	169.56	3	508.68
GDEB-18-325	18	3.25	183.69	3	551.07
GDEB-18-350	18	3.5	197.82	3	593.46
GDEB-18-375	18	3.75	211.95	3	635.85
GDEB-18-400	18	4	226.08	3	678.24
GDEB-20-200	20	2	125.60	3	376.80
GDEB-20-225	20	2.25	141.30	3	423.90
GDEB-20-250	20	2.5	157.00	3	471.00
GDEB-20-275	20	2.75	172.70	3	518.10
GDEB-20-300	20	3	188.40	3	565.20
GDEB-20-325	20	3.25	204.10	3	612.30
GDEB-20-350	20	3.5	219.80	3	659.40
GDEB-20-375	20	3.75	235.50	3	706.50
GDEB-20-400	20	4	251.20	3	753.60
GDEB-23-200	23	2	144.44	3	433.32
GDEB-23-225	23	2.25	162.50	3	487.49
GDEB-23-250	23	2.5	180.55	3	541.65
GDEB-23-275	23	2.75	198.61	3	595.82
GDEB-23-300	23	3	216.66	3	649.98
GDEB-23-325	23	3.25	234.72	3	704.15
GDEB-23-350	23	3.5	252.77	3	758.31
GDEB-23-375	23	3.75	270.83	3	812.48
GDEB-23-400	23	4	288.88	3	866.64
GDEB-25-200	25	2	157.00	3	471.00
GDEB-25-225	25	2.25	176.63	3	529.88
GDEB-25-250	25	2.5	196.25	3	588.75
GDEB-25-275	25	2.75	215.88	3	647.63
GDEB-25-300	25	3	235.50	3	706.50
GDEB-25-325	25	3.25	255.13	3	765.38
GDEB-25-350	25	3.5	274.75	3	824.25

GDEB-25-375	25	3.75	294.38	3	883.13
GDEB-25-400	25	4	314.00	3	942.00
GDEB-30-200	30	2	188.40	3	565.20
GDEB-30-225	30	2.25	211.95	3	635.85
GDEB-30-250	30	2.5	235.50	3	706.50
GDEB-30-275	30	2.75	259.05	3	777.15
GDEB-30-300	30	3	282.60	3	847.80
GDEB-30-325	30	3.25	306.15	3	918.45
GDEB-30-350	30	3.5	329.70	3	989.10
GDEB-30-375	30	3.75	353.25	3	1059.75
GDEB-30-400	30	4	376.80	3	1130.40
GDEB-35-200	35	2	219.80	3	659.40
GDEB-35-225	35	2.25	247.28	3	741.83
GDEB-35-250	35	2.5	274.75	3	824.25
GDEB-35-275	35	2.75	302.23	3	906.68
GDEB-35-300	35	3	329.70	3	989.10
GDEB-35-325	35	3.25	357.18	3	1071.53
GDEB-35-350	35	3.5	384.65	3	1153.95
GDEB-35-375	35	3.75	412.13	3	1236.38
GDEB-35-400	35	4	439.60	3	1318.80
GDEB-40-200	40	2	251.20	3	753.60
GDEB-40-225	40	2.25	282.60	3	847.80
GDEB-40-250	40	2.5	314.00	3	942.00
GDEB-40-275	40	2.75	345.40	3	1036.20
GDEB-40-300	40	3	376.80	3	1130.40
GDEB-40-325	40	3.25	408.20	3	1224.60
GDEB-40-350	40	3.5	439.60	3	1318.80
GDEB-40-375	40	3.75	471.00	3	1413.00
GDEB-40-400	40	4	502.40	3	1507.20

7) Raw materials

Raw materials (Drug application composition)

No.	Part name	Material	Standards	Ratio	Body contact	remarks
1	Drug coating	Paclitaxel	EP	50%(3μg/㎟)	Yes (Circulating blood)	
		Shellac	In house 1	25%		
		D-α-Tocopherol polyethylene glycol succinate	In house 2	25%		

Raw materials (Balloon catheter)

No	Part name	Material	Standards	Ratio	Body contact	remarks
1	End tip	Hexanedioic acid, polymer with azacyclotridecan-2-one and.alpha.-	In house 3	99.9%	Yes (Circulating	

		hydro-.omega. -hydroxypoly(oxy-1,4-butanediyl)				blood)
		Thermoplastic resin+colorant		In house 4	0.1%	
2	Balloon	Polyamide 12		In house 5	50%	Yes (Circulating blood)
		Hexanedioic acid, polymer with azacyclotridecan-2-one and.alpha.-hydro-.omega. -hydroxypoly(oxy-1,4-butanediyl)		In house 6	50%	
3	Radiopaque marker	Platinum-iridium alloy		In house 7	Pt:90%, Ir:10%	No
4	Proximal shaft	Stainless steel alloy 304		ASTM A240	99.9%	Yes (Circulating blood)
		Toluene Mixture		In house 8	0.1%	
5	Distal shaft	Anterior	Hexanedioic acid, polymer with azacyclotridecan-2-one and.alpha.-hydro-.omega. -hydroxypoly(oxy-1,4-butanediyl)	In house 9	100%	Yes (Circulating blood)
		Posterior	Azacyclotridecan-2-one, homopolymer	In house 10	100%	Yes (Circulating blood)
6	Hub, Strain relief	Polycarbonate		In house 11	99.998%	No
		Solvent Blue 78		In house 12	0.002%	
7	Hydrophilic coating-first layer	Etylene acrylic acid copolymer		In house 13	72.57%	Yes (Circulating blood)
		Hexamethylene diisocyanate homopolymer		In house 14	22.25%	
		Propylene glycol monomethyl ether acetate		In house 15	4.66%	
		Polyfunctional aziridine		In house 16	0.52%	
	Hydrophilic coating-top layer	Hyaluronic acid sodium salt		In house 17	100%	Yes (Circulating blood)
8	Guidewire tube	Outer	Hexanedioic acid, polymer with azacyclotridecan-2-one and.alpha.-hydro-.omega. -hydroxypoly(oxy-1,4-butanediyl)	In house 6	95.24%	Yes (Circulating blood)
			C.I. pigment black 7	In house 18	4.76%	
		Middle	Maleic anhydride grafted polyethylene	In house 19	100%	No
		Inner	1-hexene, polymer with	In house 20	100%	Yes

			ethene			(Circulating blood)	
9	Protector tube	Polytetrafluoroethylene		In house 21	100%	No	Concurrent use
		High density polyethylene		In house 24	100%		
10	Storage mandrel	Stainless steel alloy 304		ASTM A240	100%	No	
11	Dispenser tube	High density polyethylene		In house 22	100%	No	
12	Compliance chart	Polyethylene terephthalate		In house 23	100%	No	

7.2. Intended use for investigational device

■ Intended use for Test device(Genoss® DCB)

Approved intended use : This is a balloon catheter used in percutaneous coronary intervention (PCI) and is used to treat in-stent restenosis due to late lumen loss of stents with a reference vessel diameter of 2.0 mm to 4.0 mm.

It is used to treat patients with de novo lesion stenosis with a diameter of 2.0 mm to 4.0 mm for percutaneous coronary angioplasty (PTCA).

7.3. Instruction for use and precaution of investigational device

■ Instruction for use and precaution of Test device(Genoss® DCB)

A. Preparation before use

▶ Materials required for the procedure
- Rapid Exchange PTCA balloon catheter
- Appropriate guiding catheter
- 10~20cc syringe 2~3ea
- guide wire 1ea with a diameter of 0.36 mm (0.014 inch) or less
- Rotary hemostatic valve with appropriate internal diameter
- Contrast medium diluted 1:1 with normal saline
- Pressure device 1ea
- Stopcock(at least 3-way)
- Appropriate anticoagulants and antiplatelet agents

▶ Preparation before use
- Before opening the product, check that the packaging container is not damaged or that the packaging is completely blocked from external air before use.
- Parts that require sterilization before use are sterilized according to sterilization conditions and established methods.

- Check that there are no missing components in the product.
- Be careful not to open the packaging until just before use.
- Remove the balloon catheter from the dispenser without bending or kinking it.

B. How to use and operation sequence

※ Precautions: Before drug-coated balloon catheter (DCB) intervention, always perform pre-dilation with a standard balloon. The pre-dilatation method is the same as the use and operation sequence of the drug-coated balloon catheter (DCB) as shown below, and the DCB is applied after fully modifying the plaque with a plain balloon of the optimal size (balloon to artery ratio 1:1).

* Pre-dilation : This is a procedure to enlarge the target lesion using a standard balloon that is not coated with drugs before DCB treatment. DCB is applied after completely improving the plaque of the lesion with a standard balloon of the optimal size (balloon to artery ratio 1:1). If standard semi-compliant balloons fail to expand, high-pressure non-compliant balloons or cutting and scoring balloons are recommended.

- Preparation of balloon catheter for percutaneous coronary angioplasty

1 Separate the dispenser and balloon catheter from the packaging material and place them on the sterile filter.

2 Carefully separate the balloon catheter from the dispenser.

3 Carefully separate the balloon protection tube and stylet to avoid damaging the balloon area.

- Cleaning the guide wire passage pipe

4 Attach an appropriately sized irrigation needle to a syringe filled with sterile saline.

5 Insert the needle into the distal end of the balloon catheter and clean the inside of the guide wire.

6 Remove the cleaning needle and syringe.

- Removal of air within the catheter inflation tube.

7 Connect the hub and cock of the balloon catheter.

8 Connect a 10ml or 20ml syringe filled with 3ml of contrast medium to the cock, pull the plunger for 30 seconds, and suck out the gas.

9 Lock the cock. Remove the syringe and empty all air from the canister.

10 실 Reconnect the syringe, open the cock, and suck until no more bubbles form. Place the syringe at normal pressure. At this time, be careful not to let air enter the system. Close the cock and remove the syringe.

- Connection of inflation device

11 Prepare the inflation device according to the manufacturer's recommendations and

instructions and remove air from the inflation device.

12 Connect the inflation device to the cock.

WARNING: Do not allow air to enter the system.

13 Remove all air remaining in the system through the cock. Make it negative pressure and set it aside to use.

14 Connect the hemostatic valve to the hub of the guiding catheter located within the vascular structure.

15 Perform fluoroscopic examination according to the percutaneous coronary angioplasty method and position the guide wire.

16 Backload the proximal end of the guide wire to the distal tip of the balloon catheter until the guide wire extends 25 cm from the distal end of the catheter.

17 Carefully insert the balloon catheter through the hemostatic valve and advance the balloon catheter.

18 In order to confirm when the distal tip of the balloon catheter reaches the distal tip of the guiding catheter, insert the balloon catheter through the guiding catheter using fluoroscopy.

※ caution: You can check that the balloon catheter is getting closer to the distal end of the guiding catheter through the two markers at the proximal end.

19 A balloon catheter is introduced into the coronary artery and guided along the guide wire in the direction of the lesion.

※ caution: Minimize the time from the time the drug-coated catheter (DCB) contacts the blood vessel until it is inflated to the nominal pressure to within 3 minutes. If 3 minutes are exceeded, remove the failed DCB, replace it with a new product, and perform the procedure again.

20 An impermeable balloon marker confirms the position of the balloon in the lesion.

- Balloon inflation

21 Open the cock of the inflation device. A balloon is inflated to dilate the lesion according to percutaneous coronary angioplasty method. At this time, the drug-coated balloon catheter should be 2-3 mm longer on the side than the pre-dilated standard balloon, and the balloon diameter should match the reference vessel diameter.

※ cautions: When expanding the balloon, apply appropriate pressure (8-12 atm) to ensure that the drug coated on the balloon surface adheres well to the blood vessel wall, and the holding time after inflation is 60 seconds. At this time, if the patient has difficulty enduring the maintenance time after inflation, it can be performed twice (2 x 30 seconds).

22 In particular, if the lesion persists, the balloon is inflated by gradually increasing the pressure until the lesion disappears to improve it.

23 After dilatation, blood flow in the distal coronary artery is assessed by angiography through a guiding catheter.

- Removal process

The Genos balloon catheter for percutaneous coronary angioplasty is designed so that the operator can quickly remove the balloon catheter by himself.

24 Unscrew the hemostasis valve.

25 Hold the guide wire and hemostatic valve while holding the balloon area with the other hand.

26 Maintain the guide wire position within the coronary artery to avoid moving the guide wire. Then, the balloon catheter begins to be pulled out of the guiding catheter.

※ **Caution: We recommend monitoring the guidewire position through fluoroscopy during exchange.**

27 Pull the balloon catheter until it reaches the guide wire exit point. Carefully remove the distal end of the flexible balloon catheter from the guide wire while maintaining the guide wire across the lesion. Close the hemostasis valve.

※ **Caution: If difficulty occurs while removing the catheter, remove the entire system immediately. That is, the guiding catheter, guide wire, and balloon catheter are removed at the same time.**

28 Completely remove the balloon catheter from the guide wire.

29 Please follow the manufacturer's instructions for use or prepare the balloon catheter for subsequent use as described above.

C. How to store and manage after use

Since this product is a disposable product, used products should not be re-sterilized or reused, and should be discarded in accordance with regulations after use.

- Precautions for use

A. Contraindications

In general, contraindications to using this product and balloon catheter for percutaneous coronary angioplasty are as follows.

1. Patients with sensitivity or allergic reaction to paclitaxel and/or delivery matrix (Shellac, Vitamin E-TPGS)
2. Patients with severe allergic reactions to contrast media
3. Completely occluded lesion
4. Experience of cardiogenic shock
5. Patients with coronary artery attacks in situations where no specific stenosis occurs; those with a hemorrhagic tendency or a history of known allergy to aspirin, heparin, ticlopidine, clopidogrel, or any antiplatelet or anticoagulant.
6. Pregnant women
7. Patients with blood vessel diameter less than 2 mm

8. Patients who have suffered an acute myocardial infarction (AMI) within the last week
9. Treatment of the unprotected left main coronary artery
10. Patients with lesions that prevent complete inflation of the angioplasty balloon
11. Patients with ejection fraction less than 30%

B. General precautions

This product must be used by a physician who is appropriately trained or skilled in the PCI procedure. Please use this product after carefully reading the user manual. This product is sterilized with ethylene oxide. Since it is a sterilized product, ensure that it remains sterile during the procedure, and do not use it after the expiration date. Check the contents before use and do not use if the packaging shows signs of damage or moisture. Users must confirm that there are no functional problems with the balloon catheter before intervention. It must be confirmed and guaranteed that the specifications of the balloon catheter to be used are appropriate for the relevant intervention. Only specialists who have received complete training and education on balloon catheters for percutaneous coronary angioplasty can use the balloon catheter system. Use caution during manipulation to reduce the possibility of peeling off the drug coating on the balloon, accidental breakage of the balloon catheter, or bending or kinking of the distal end. Appropriate anticoagulants and vasodilator medications should be used prior to catheter insertion. Anticoagulant treatment must be continued for a certain period of time after the procedure, as determined by the doctor. Care must be taken to maintain the position of the guiding catheter tip while manipulating the balloon catheter. When inserting or exchanging a balloon catheter, clean the guide wire thoroughly to ensure smoother movement of the inserted balloon catheter.

C. Precaution when handling

This product is intended and designed for single-use use only. It is used only on the same patient, and reuse, reprocessing, and re-sterilization may damage the product or cause infection or cross-infection in the patient due to contamination of the product, and may cause pain, suffering, and death in the patient. After use, products and packaging must be disposed of according to administrative procedures in accordance with hospital and government policies. To reduce vessel damage during surgery, the inflation diameter of the balloon should be similar to the diameter of the distal vessel proximal to the stenotic vessel segment. When performing percutaneous transluminal coronary angioplasty in patients for whom coronary artery bypass grafting is impossible, serious consideration must be given to whether or not the surgery should be performed. Because the treatment of this patient population carries special risks, it is recommended that hemodynamic support be provided whenever possible while performing percutaneous coronary angioplasty. This product is recommended for use in high-performance fluoroscopic examination environments. It is prohibited to insert or remove a balloon catheter without the balloon being fully deflated. If you feel great resistance during manipulation, stop the operation, determine the cause of the resistance, and deal with the problem. During use,

the balloon must not exceed its rated burst pressure (RBP). To prevent excessive pressure from being applied to the balloon during surgery, check the pressure gauge of the pressure device regularly. Percutaneous coronary angioplasty should be performed in a hospital where emergency coronary artery bypass grafting can be performed immediately. An appropriate balloon inflation medium should be used (such as contrast medium diluted 1:1 with normal saline). Do not use air or other gases to inflate the balloon. Additionally, it is prohibited to bring organic solvents into contact with the balloon catheter (alcohol, etc.).

D. Possible side effects/complications

'1.25. See 'Expected adverse events'

8. SELECTION/EXCLUSION CRITERIA AND CALCULATION BASIS FOR NUMBER OF SUBJECTS

8.1. Target disease

Patients who need intervention due to a de-novo lesion in a coronary artery with a diameter of 2.0 mm to 4.0 mm

8.2. Selection/exclusion criteria

8.2.1. Inclusion criteria

You must meet all of the following inclusion criteria to participate in this clinical trial.

Inclusion criteria:

1. Adults over 19 years old
2. When intervention is required due to a new lesion in the coronary artery [17]
   * *Coronary artery lesion that has never been treated with any interventional procedure (e.g., plain old balloon angioplasty (POBA), stent, rotablation, laser procedure, etc.)*
3. In case of stable angina, unstable angina, or silent ischemia [18]
4. If you are a woman of childbearing age, you agree to use one or more clinically appropriate contraceptive methods* during the test period.

* *Clinically appropriate contraception is defined as "[an intrauterine device (e.g. loop, Mirena), chemical barrier method (spermicide), or subcutaneous implant contraceptive device (e.g. Implanon)] plus a physical barrier method (male or female), tubal surgery, or laparoscopic contraception(a type of tubal ligation).*

5. A person who voluntarily agrees to participate in a clinical trial and is willing to comply with

the subject compliance requirements

Inclusion criteria in coronary angiography:

6. If there is significant coronary artery stenosis (>50% diameter stenosis on coronary angiography) [18]
7. When the length of the lesion on coronary angiography is less than 34 mm and the reference vessel diameter of the coronary artery is between 2.0 mm and 4.0 mm.[9, 18, 19]

8.2.2 Exclusion criteria

If you meet any of the following exclusion criteria, you cannot be registered for a clinical trial.

Exclusion criteria:

1. Persons with ST segment elevation myocardial infarction (STEMI)
2. Persons with known hypersensitivity or contraindications to the following drugs or substances

• aspirin, • heparin, • Ticagrelor, • Contrast media(Iopromide, etc.)	• clopidogrel, • Prasugrel, • paclitaxel,

(However, even subjects with hypersensitivity to contrast media can be registered if they can be controlled with steroids and pheniramine, but cases with known anaphylaxis are excluded)

3. Patients with platelet aggregation or disorders at risk of increased bleeding, such as gastrointestinal ulcers, which limit platelet aggregation inhibitor therapy and anticoagulant therapy.
4. Patients with left ventricular ejection fraction less than 30% according to echocardiography.
5. Cases not suitable for coronary angiography due to current or past severe renal failure (eGFR < 30 ㎖/min)[17]
6. In case of cardiogenic shock
7. If you are pregnant or lactating
8. If the life expectancy is less than 1 year due to a concomitant disease
9. If you have had or currently have a medical illness such as mental illness that significantly affects this clinical trial.
10. If, in the judgment of the investigator, it is not suitable for this clinical trial or may increase the risks associated with participation in the study
11. Those who are currently participating in another clinical trial or have participated in another clinical trial within 90 days of the screening date

12. In other cases, when the investigator determines that participation in the clinical trial is inappropriate because it may affect the results of the clinical trial or ethically.

☞ *Specific reasons are stated in the case report form.*

Exclusion criteria in coronary angiography:

13. In case of graft vessel lesion
14. In case of left main coronary lesion[18]
15. When it is difficult to apply an investigational device because pre-expansion is not possible or pre-expansion fails
16. If one of the following items applies after pre-expansion of the target lesion
    ① When measured as FFR (Functional measurement) ≤ 0.8 in a large vessel (limited to cases with a diameter of 3.0 mm or more) (However, FFR measurement may not be performed at the discretion of the researcher.)
    ② Those who need stent surgery due to vascular dissection that restricts blood flow
    ③ When residual stenosis is > 30%[3]
    ④ When TIMI flow is < 3

8.3. Calculation basis for number of subjects

This study plans to conduct an pilot study on 20 patients to evaluate the effectiveness and safety of the balloon-expandable coronary angioplasty catheter 'Genoss® DCB' in patients with new lesions in the coronary arteries. (As a pilot study, the number of subjects is not calculated based on hypothesis.)

9. PERIOD OF CLINICAL TRIAL

It is expected to take approximately 21 months to obtain plan approval from the Ministry of Food and Drug Safety and the Institutional Review Board, and approximately 5 additional months are expected to be required to prepare a report on the results after completion of the clinical trial.

The detailed expected duration of the clinical trial is presented below.

- Total clinical trial period (screening date of first patient ~ LPO*): approximately 21 months
  **LPO: Last Patient Out(last patient's last visit)*
  - Subject recruitment period: Approximately 12 months after obtaining approval from the Ministry of Food and Drug Safety and IRB
    ☞ *May change depending on the speed of subject registration.*
  - Clinical trial period for each subject: approximately 6 months (maximum 7 months)
    - Screening period: up to 1 month

- Treatment and follow-up period: 6 months

- Data processing, statistical analysis, and result report writing: approximately 5 months

10. CLINICAL TRIAL

10.1. Design of clinical trial

This clinical trial is designed as a small-scale, multicenter, prospective, pilot study to evaluate the safety and effectiveness of GENOSS® DCB, a balloon-expandable angioplasty catheter, in patients with coronary artery de novo lesions measuring 2.0 mm to 4.0 mm in diameter. It will be conducted on a total of 20 people (10 per institution) at two domestic institutions.

Drug-eluting "stents" for coronary artery procedures cause blood clots due to delayed endothelial cell proliferation and local inflammatory reactions due to long-term mechanical support mechanism, so post-procedure follow-up is usually performed for 9 to 12 months[20-23]. Unlike these drug-eluting "stents" for coronary artery procedures, the "drug-coated balloon catheter", a investigational device, releases the drug quickly and uniformly and is immediately removed from the blood vessel. When the balloon is expanded, the released drug is absorbed into the blood vessel wall. It has a mechanism of action that causes sustained efficacy through absorption. Therefore, the evaluation of primary efficacy evaluation and key variables in this clinical trial were designed at 6 months, [24-25] and other variables requiring long-term safety evaluation were designed to be followed up to 6 months[16]. The primary efficacy evaluation variable of the investigational device is late lumen loss in the lesion at 6 months through coronary angiography image evaluation, and the secondary efficacy evaluation variables are device success rate, procedure success rate, restenosis rate at 6 months after the procedure, and 6 months after the procedure. It is evaluated through the incidence of target vessel failure (TVF) at the time point. Safety evaluation is confirmed through MACE (Major adverse cardiovascular event), all adverse events that occur in subjects during the clinical trial period after application of the investigational device.

10.2. Observation items, clinical test items and observation test methods

		Screening	Procedure day	Follow-up period		Unscheduled visit##
Visit		**Visit 1**	**Visit 2**	**Visit 3**	**Visit 4**	**-**
Elapsed days		**- 4w ~ 0day§**	**0day§**	**1M after procedure**	**6M after procedure**	**-**
Visit Window		**-**	**-**	**± 2w**	**± 1M**	**-**
Observation type		**Visit/ Adm**	**Adm/ Visit**	**Visit**	**Visit**	**Adm/ Visit**
Obtain written consent[1)]		√				
Selection/exclusion criteria		√	√			
Demographic survey[2)]		√				√
Medical history/surgery/procedure history[3)]		√				
Preceding medication[4)]		√				
Physical examination[5)]		√	√§§§			√
Vital signs[6)]		√	√§§§	√	√	√
Pregnancy test[7)]		√				√
Laboratory tests[8)]	General blood test	√§§		√	√	√
	Serum biochemical test	√§§		√	√	√
	Myocardial enzyme test*	√§§	√			
	Blood coagulation test	√§§				
	Glycated hemoglobin test**	√§§			√	√
	Urine test	√§§				
electrocardiogram[9)]		√§§§§	√**	√	√	√
echocaridography[10)]		√				
Coronary angiography[11)]			√		√	√
PCI (percutaneous coronary intervention) [12)]	Pre-dilation		√			
	FFR measurements		(√)ᵇ			
	Application of investigational devices		√			
revascularization[13)]						√
Check whether the device was succesful[14)]			√			
Check whether the procedure was sucessful[15)]			√#			

Check the MACE [16)]		√	√	√	√
Adverse events/serious adverse events[17)]		√	√	√	√
concomitant therapy[18)]		√	√	√	√

§ The screening visit and the procedure visit in this clinical trial can be performed on the same day, and overlapping procedures can only be performed once.

§§ (Laboratory test) If there is test data (medical record data) conducted within 4 weeks of the screening date, the test data can be used as a replacement for the screening test.

In addition, laboratory test items can be selectively performed and collected according to the standard procedures of each clinical trial institution.

(However, in case of myocardial enzyme test, it is mandatory.)

§§§Performed both before and after the procedure. Post-procedure testing can be performed within 3 days at the discretion of the researcher.

** Myocardial enzyme tests are measured twice, once between 6 and 12 hours after the procedure and once between 18 and 24 hours. If a myocardial enzyme test was not performed before the procedure, the test should be performed immediately after the procedure and measured a total of three times. If elevated levels are observed, follow-up testing is performed according to the institution's standard procedures.*

§§§§ (Electrocardiogram test) If there is test data (medical record data) performed within the screening 'elapsed days' period, the test data can be used as a replacement for the screening test.

***The glycated hemoglobin test may not be performed at the discretion of the researcher.*

****On the day of the procedure, the electrocardiogram is measured 24 hours (±6 hours) after the procedure.*

♭ Implemented only in cases of large vessels.

 # Check at the time of discharge.

##Refers to hospitalization or visit to a clinical trial institution for revascularization of the target lesion.

1) Obtain written consent

Written consent must be obtained before all clinical trial-related activities, and the investigator must inform the subject or guardian (subject representative) of the purpose and content of the clinical trial, including the risks and benefits of participating in the clinical trial, in simple terms before obtaining written consent.

2) Demographic survey

Date of birth, gender, height, weight, drinking history, and smoking history are investigated. However, at the end visit (visit 4 or unscheduled visit), only drinking and smoking history are investigated.

3) Medical history/surgery/procedure history

Medical history (past and current medical history) and procedure/surgery history for 6 months prior to the screening date are investigated. In case of angina pectoris in the medical history, The Canadian Cardiovascular Society (CCS) Class is additionally collected. However, the medical history, surgery, and procedure history that must be investigated for screening are investigated based on

the time points indicated in the selection/exclusion criteria section.

4) Preceding medication

Drugs administered more than 4 weeks prior to the screening date are investigated. However, prerequisite drugs that must be investigated for screening are investigated based on the time points indicated in the selection/exclusion criteria section.

5) Physical examination

Investigate information related to appearance, skin, head/neck, chest/lungs, heart, abdomen, urinary/reproductive system, extremities, musculoskeletal system, nervous system, lymph nodes, and other body organs.

6) Vital signs

Measure body temperature, blood pressure* (systolic/diastolic), and pulse*.

*Blood pressure and pulse are measured in a sitting position after resting for 5 minutes.

7) Pregnancy test

A pregnancy confirmation test is performed using Urine hCG (or Serum β-hCG), and women who are confirmed to be pregnant at the time of screening (Visit 1) cannot participate in this clinical trial and at the end visit (Visit 5 or unscheduled visit). If pregnancy is confirmed, follow-up is conducted until delivery or termination of pregnancy.

8) Laboratory tests

Laboratory test items are classified into normal and abnormal according to the standards set by the clinical trial institution, and in case of abnormality, they are classified and recorded as NCS (Not Clinically Significant) and CS (Clinically Significant) at the discretion of the researcher. If CS is confirmed, it should be recorded as an adverse event. Specific test items for laboratory tests are as follows, and laboratory test items can be selectively performed and collected according to the standard procedures of each clinical trial institution. However, in the case of myocardial enzyme testing, it is mandatory.

Table 2. Laboratory test items

	측정 항목
General blood test	White blood cell(WBC), red blood cell(RBC), hemoglobin(Hb), hematocrit(Hct), platelet count(PLT)
Serum biochemical test	**Liver function:** alkaline phosphatase(ALP), aspartate aminotransferase(AST), alanine transaminase(ALT), lactate dehydrogenase(LDH), total bilirubin, gamma-glutamyl transferase(γ-GT) **Metabolic function:** total cholesterol, glucose, total protein, albumin,

	triglyceride, serum creatinine, high density lipoprotein(HDL)-cholesterol, low density lipoprotein(LDL) cholesterol, blood urea nitrogen(BUN), e-glomerular filtration rate(eGFR) **Electrolytes:** Na, K, Cl, Ca
Myocardial enzyme test	Creatine kinase(CK), creatine kinase myocardial band(CK-MB), Troponin-I(or Troponin-T)
Blood coagulation test	activated partial thromboplastin time(aPTT), prothrombin time(PT)
Glycated hemoglobin test	HbA1c
Urine test	Protein, Glucose, Ketone, Blood

9) Electrocardiogram

The subject's electrocardiogram is measured and the occurrence of adverse events such as myocardial infarction or arrhythmia is observed.

10) Echocardiography

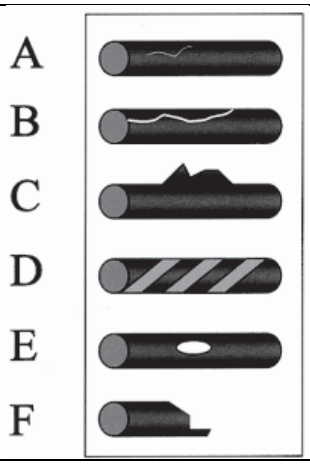
It can be replaced with echocardiography results from within 6 months before the screening date, and if there are left ventricular ejection fraction results, the most recent existing data can be used without retesting. If there is no existing data, the left ventricular ejection fraction results are confirmed through echocardiography.

11) Percutaneous coronary angiography

Coronary angiography is performed before coronary intervention (PCI) to determine whether the selection/exclusion criteria are appropriate, target lesion selection, and baseline evaluation of the lesion. After the procedure, coronary angiography is performed to evaluate effectiveness. During coronary angiography, the following items are collected.

Table 3. coronary angiography observation items and collection time

Related to target vessel	- Number of lesions	immediately before the procedure
	- Location of vessel lesion: LAD/LCX/RCA	immediately before the procedure
Related to target lesion	- Whether blood vessel dissection is present - NHLBI classification * Vascular dissection is described according to the NHLBI (The National Heart, Lung and Blood Institute) classification. (see below)	Immediately after the procedure

		
	- Minimum lumen diameter (MLD, mm), reference vessel diameter (RVD, mm)	Immediately before the procedure, immediately after the procedure, 6 months after the procedure, unscheduled visits
	- Stenosis rate (%)	Immediately before the procedure, immediately after the procedure, 6 months after the procedure, unscheduled visits
	- Length of lesion (mm)	Immediately before the procedure
	- Presence of eccentric lesion	Immediately before the procedure
	- Lesion type (type A, B1, B2, C) according to ACC/AHA classification	Immediately before the procedure

12) Percutaneous coronary intervention (PCI)

Only subjects who meet all selection/exclusion criteria during PCI are registered, and the following items are collected according to each procedure.

Table 4. Coronary intervention observation items

Pre-dilation	- Whether the dictionary expansion was successful or not - Whether blood vessel dissection is present 혈관 박리 여부 - NHLBI classification * Vascular dissection is described according to the NHLBI (The National Heart, Lung and Blood Institute) classification (see above) - Minimum lumen diameter (MLD, mm) - Reference vessel diameter (RVD, mm) - Residual stenosis (after pre-dilatation)

	- Check TIMI grade flow(refer to Table 7)
FFR measurements	- FFR measurement value (if the blood vessel containing the target lesion is a large vessel (3.0mm or more))
Application of investigational device	- Number of medical devices applied for clinical trials - Balloon diameter (mm) - Balloon length (mm) - Balloon inflation pressure (atm) - Time to reach target lesion (sec) - Inflation time (sec)

Table 5. TIMI grade flow Evaluation standard

Grade	평가기준
TIMI 0 flow	A state in which there is no perfusion into the tissue. (State in which no staining by contrast agent occurs within the tissue)
TIMI 1 flow	A condition in which intramyocardial contrast material is stained but is not removed and continues to remain.
TIMI 2 flow	A condition in which contrast agent stains the myocardium but is removed only after three or more cardiac cycles have elapsed.
TIMI 3 flow	A condition in which staining and removal of contrast agent within the myocardium is completed quickly and completely within three cardiac cycles.

13) Revascularization

Ischemia-driven target lesion revascularization (ID-TLR) or TVR is performed when the treated target lesion has an internal diameter stenosis of more than 50% and symptoms of angina pectoris, myocardial ischemia is suspected in objective tests, or both exist. At this time, the stenosis rate before revascularization is recorded in the case report form.

14) Check whether the device was successful or not

The success of the investigational device in reaching the target lesion, success in expansion and contraction operation, rupture, and success in retrieval are recorded in the case report form.

15) Check whether the procedure was successful

During the hospitalization period, TLF is checked and recorded in the case report form.

16) Check for MACEMACE

Cardiac death, myocardial infarction (ST-segment elevation myocardial infarction, non-ST-segment elevation myocardial infarction), target vessel thrombosis, and vascular revascularization (ID-TLR, TVR) are checked and recorded (more details in '12.2.1. Safety endpoints').

17) Adverse events/serious adverse events

When an adverse event or serious adverse event occurs, all confirmed matters, such as the adverse

event name, start and end date, severity, causality with the investigational device, treatment details and results, are recorded in the case repot form (Refer to the '15. Safety evaluation criteria, evaluation methods and reporting methods including side effects' section).

18) Concomitant therapy

When investigating concomitant medications, record drugs whose dose or route has newly changed since the screening visit and drugs administered. Due to the nature of this clinical trial, dual antiplatelet therapy (DAPT) drugs that will be prescribed after the procedure may affect the effectiveness and safety, so new drugs will be prescribed in consideration of the subject's condition. At this time, record the drug ingredient name, single dose and unit, route, frequency, administration start date, administration end date, purpose of administration, etc. When investigating concomitant therapy other than drugs, include the name, start date, end date, and purpose of the treatment. Subjects will receive concomitant medication according to the guidelines below, but the drug, dosage, and dosage may be determined at the discretion of the investigator.

Drugs allowed in concomitant:

① Before the procedure

Before the procedure, the usage and dosage of aspirin, Clopidogrel, Ticagrelor, and Prasugrel are administered according to the investigator's decision. If there is an allergy or side effect to clopidogrel or there is no drug, Administer ticlopidine. Additionally, antiplatelet agents such as cilostazol may be added at the discretion of the researcher.

② During the procedure

During the procedure, the usage and dosage of heparin are administered according to the investigator's decision, and antiplatelet agents such as glycoprotein IIb/IIIa inhibitors (abciximab, tirofiban) or anti-thrombin IIb/IIIa are also administered at the discretion of the operator.

③ After the procedure

After the procedure, the usage and dosage of aspirin, clopidogrel, ticagrelor, and prasugrel are administered as determined by the researcher. In case of hypersensitivity to clopidogrel, ticlopidine is administered. use. In general, dual antiplatelet therapy is performed for up to 6 months after the procedure, but if the period needs to be adjusted depending on the patient's condition, it may be changed.

Drugs with caution in concomitant:

- Caution must be exercised, when using CYP3A4 and/or CTP2C8 substrates, including terfenadine, cyclosporine, lovastatin, midazolam, and ondansetron, or drugs containing hyper-plasma protein binding (PPB) (especially sulfonureas, coumarin-type anticoagulants, salicylates, sulfonamides, dickytoxin).
- Possible interactions between Paclitaxel and additional drugs (e.g. anticancer drugs) should be referred to the relevant instructions for use.

10.3. Clinical trial procedures

■ Before the procedure

< Visit 1: Screening – 4 weeks to 0day, Visit/Adm>

Patients with de novo lesions in the coronary arteries who are judged to require interventional procedures will be referred to this clinical trial. Patients who voluntarily sign a written consent form after receiving a sufficient explanation about the clinical trial will undergo a screening test.

During the screening visit (Visit 1), the following items are observed and inspected in addition to the selection/exclusion criteria.

- Demographic survey
- Medical history/surgery/procedure history
- Premedication
- Physical examination
- Vital signs
- Pregnancy test
- Laboratory tests: general blood test, serum biochemical test, myocardial enzyme test, blood coagulation test, glycated hemoglobin test, urine test.

☞ *It is carried out in accordance with the standard procedures of each clinical trial institution. (However, in case of myocardial enzyme test, it is mandatory.)*

- Electrocardiogram
- Echocardiography

☞ *If there are test results within 6 months prior to the screening date, it can be omitted.*

Potential subjects who meet all selection/exclusion criteria (items that can be confirmed by coronary angiography and whether pre-dilatation is successful or not are confirmed on the procedure day) except those required to be confirmed on the day of the procedure through a screening test are scheduled for hospitalization and procedure date. The patient is hospitalized on the scheduled date and receives pre-procedure treatment and drug therapy (aspirin and P2Y12 inhibitors) (generally, the patient is admitted the day before the procedure, but the hospitalization date can be changed at the discretion of the investigator.)

■ Procedure day

<Visit 2: procedure day – 0day, Adm/Visit>

The investigator performs the following tests before the procedure and checks whether the selection/exclusion criteria for the lesion are met through coronary angiography.

- Physical examination

- Vital signs

After this, dictionary expansion is performed according to the procedure below.

> * Pre-dilation: This is a procedure to expand the target lesion using a standard balloon that is not coated with drugs before the DCB procedure. Apply DCB after completely improving the plaque of the lesion with a standard balloon of optimal size (balloon to artery ratio 1:1). If expansion of a standard semi-compliant balloon fails, a high-pressure non-compliant balloon or a cutting and scoring balloon is recommended.

If pre-dilation is not performed or pre-dilation fails, or if vascular dissection (exclusion criteria 17-②) occurs even if pre-dilation is successful and stent surgery is required, the subject will be processed as a screening failure and the institution Alternative treatments are performed according to standard procedures.

If pre-expansion is successful, the success of pre-expansion is recorded in the case report form.

1) In the case of large vessels (limited to those with a diameter of 3.0 mm or more), the myocardial fractional flow reserve (FFR) is measured, and if the FFR measurement value is > 0.8, it is registered in this clinical trial.

☞ *If the FFR measurement value is ≤ 0.8, the patient will be excluded from screening and alternative treatment (DES (Drug elution stent) insertion, etc.) will be performed according to institutional procedures.*

2) In case of small vessels (diameter over 2.0 mm ~ less than 3.0 mm), they are registered in this clinical trial without FFR measurement.

※ *If there are two or more lesions that meet the inclusion criteria, the lesion with the narrowest minimum lumen diameter is selected as the target lesion.*

Afterwards, the assigned investigational device is applied only to subjects who meet the selection and exclusion criteria. After applying the investigational device, the procedure is terminated when observation and testing for adverse events and effectiveness evaluation are completed. At this time, the method of applying the investigational device is as follows (for detailed usage of the investigational device, refer to section '8.3. How to use the investigational device and precautions for use').

> <How to apply medical devices for clinical trial>
> Minimize the time from when the DCB contacts the blood vessel until it expands to the nominal pressure to within 3 minutes. If 3 minutes are exceeded, remove the failed DCB, replace it with a new product, and perform the procedure again. The drug-coated balloon catheter should be 2-3 mm longer on the side than the pre-dilated standard balloon, and the balloon diameter should match the reference vessel diameter.

After completing the procedure, observe and inspect the following items.

- Physical examination
- Vital signs
- Electrocardiogram
  : On the day of the procedure, the electrocardiogram is measured 24 hours (±6 hours) after the procedure.
- Laboratory test: Myocardial enzyme test
  : Myocardial enzyme tests are measured twice, once between 6 and 12 hours after the procedure and once between 18 and 24 hours. If a myocardial enzyme test was not performed before the procedure, the test should be performed immediately after the procedure and measured a total of three times. If elevated levels are observed, follow-up testing is performed according to the institution's standard procedures.
- Check whether the device was successful or not
- Check whether the procedure was successful
  : *Check at the time of discharge.*
- Check for MACE
- Adverse events/serious adverse events
- Concomitant therapy

Subjects will continue to be hospitalized for progress observation, and the time of discharge will be determined by the investigator according to the institution's standard procedures.

■ Follow-up period

<Visit 3: 1 month ± 1 week after procedure, Visit>

When the subject visits the hospital 1 month after the procedure, the following items are observed and examined.

- Vital signs
- Laboratory tests: general blood test, serum biochemical test

☞ *It is carried out in accordance with the standard procedures of each clinical trial institution.*

- Electrocardiogram
- Check for MACE
- Adverse events/serious adverse events
- Concomitant therapy

<Visit 4: 6 months ± 2 weeks after procedure, Visit>

When the subject visits the hospital 6 months after the procedure, the following items are observed and examined.

- Vital signs

- Laboratory tests: general blood test, serum biochemical test, glycated hemoglobin test

☞ *It is carried out in accordance with the standard procedures of each clinical trial institution.*

- Electrocardiogram
- Coronary angiography
  : Acquired coronary angiography images are stored for validity evaluation.
- Check for MACE
- Adverse events/serious adverse events
- Concomitant therapy

After completing the follow-up evaluation at 6 months after the procedure, if no adverse events have occurred or if all adverse events that have already occurred are resolved, the subject's clinical trial visit is terminated. However, if the investigator determines that follow-up is no longer necessary for a subject whose adverse event has not been completely resolved, the subject's visit may be terminated 6 months after the procedure.

☞ *If there are any adverse events or residual symptoms due to adverse events even after the end of the clinical trial, medical measures will be taken in accordance with the institution's standard medical guidelines (refer to section '16.6. Treatment and treatment standards for subjects after clinical trial' of the clinical trial protocol).*

※ *If combination therapy is administered during the clinical trial period, it must be recorded in the case report form.*

※ *Coronary angiography images taken during the procedure and follow-up period are collectively delivered to the evaluator for effectiveness evaluation.*

■ Unscheduled Visit

During the follow-up period, revascularization (ID-TLR or TVR) is performed if the target lesion has stenosis of more than 50% and angina or myocardial ischemia is suspected.

☞ *Subjects who have undergone revascularization of the target lesion will visit on an unscheduled visit date for examination and observation.*

During unscheduled visits, observe and inspect the following items.

- Demographic survey
- Physical examination
- Vital signs
- Pregnancy test
- Laboratory tests: general blood test, serum biochemical test, glycated hemoglobin test

☞ *It is carried out in accordance with the standard procedures of each clinical trial institution.*

- Electrocardiogram

- Coronary angiography (before revascularization)
  - Minimum lumen diameter (MLD)
  - Reference vessel diameter (RVD)
- Check for MACE
- Adverse events/serious adverse events
- Concomitant therapy

10.4. Concomitant therapy

When investigating concomitant medications, record drugs whose dose or route has newly changed since the screening visit and drugs administered. Due to the nature of this clinical trial, dual antiplatelet therapy (DAPT) drugs that will be prescribed after the procedure may affect the effectiveness and safety, so new drugs will be prescribed in consideration of the subject's condition. At this time, record the drug ingredient name, single dose and unit, route, frequency, administration start date, administration end date, purpose of administration, etc. When investigating concomitant therapy other than drugs, include the name, start date, end date, and purpose of the treatment. Subjects will receive concomitant medication according to the guidelines below, but the drug, dosage, and dosage may be determined at the discretion of the investigator..

Concomitant allowed therapy

■ Drugs allowed in concomitant

① Before the procedure

Before the procedure, the usage and dosage of aspirin, Clopidogrel, Ticagrelor, and Prasugrel are administered according to the investigator's decision. If there is an allergy or side effect to clopidogrel or there is no drug, Administer ticlopidine. Additionally, antiplatelet agents such as cilostazol may be added at the discretion of the researcher.

② During the procedure

During the procedure, the usage and dosage of heparin are administered according to the investigator's decision, and antiplatelet agents such as glycoprotein IIb/IIIa inhibitors (abciximab, tirofiban) or anti-thrombin IIb/IIIa are also administered at the discretion of the operator.

③ After the procedure

After the procedure, the usage and dosage of aspirin, clopidogrel, ticagrelor, and prasugrel are administered as determined by the researcher. In case of hypersensitivity to clopidogrel, ticlopidine is administered. use. In general, dual antiplatelet therapy is performed for up to 6 months after the procedure, but if the period needs to be adjusted depending on the patient's condition, it may be changed.

Drugs with caution in concomitant

- Caution must be exercised, when using CYP3A4 and/or CTP2C8 substrates, including terfenadine, cyclosporine, lovastatin, midazolam, and ondansetron, or drugs containing hyper-plasma protein binding (PPB) (especially sulfonureas, coumarin-type anticoagulants, salicylates, sulfonamides, dickytoxin).
- Possible interactions between Paclitaxel and additional drugs (e.g. anticancer drugs) should be referred to the relevant instructions for use.

11. CLINICAL TRIAL EVALUATION

11.1. Effectiveness evaluation

11.1.1. Effectiveness evaluation variable

<Primary efficacy endpoint>

■ In-lesion late lumen loss (mm) at 6 months after the procedure

<Secondary efficacy endpoint>

■ Device success rate(N%)
■ Procedural success rate(N%)
■ Restenosis rate(%) at 6 months after the procedure
■ Target vessel failure(TVF) incidence rate(%) at 6 months after the procedure

11.1.2. Effectiveness evaluation criteria and methods

<Primary efficacy endpoint>

■ In-lesion late lumen loss (mm) at 6 months after the procedure

Late luminal loss within the lesion is evaluated on coronary angiography imaging at 6 months after the procedure.

① Definition of In-lesion

In-lesion is defined as the section corresponding to both ends of the lesion.

② Definition of Late lumen loss (LLL, ㎜)

LLL(mm) is defined as the value obtained by subtracting the changed vessel diameter(MLD, mm) after the follow-up period(6 months) from the dilated vessel diameter(MLD, mm) immediately after vascular intervention. Vessel diameter refers to the diameter measured based on the narrowest section within the lesion (see figure 1).

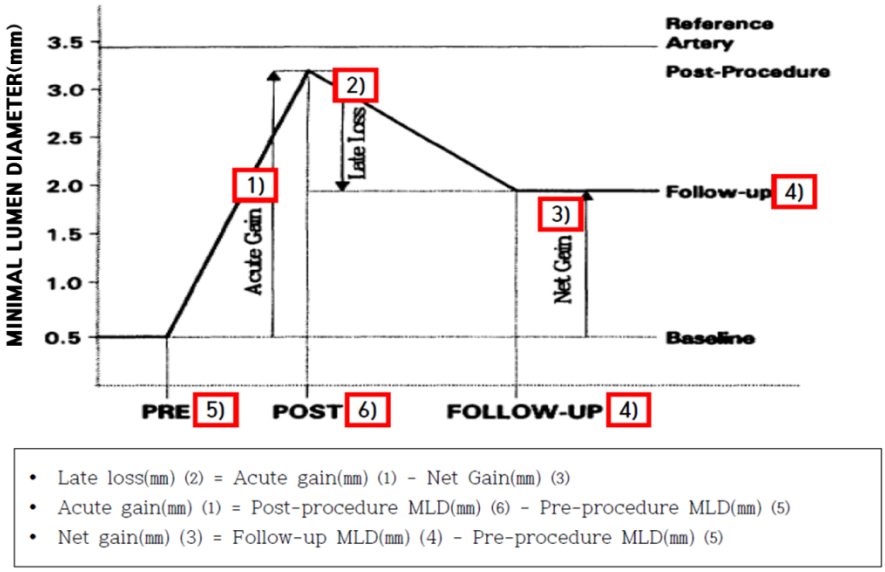


Figure 1. Definition of Late lumen loss (LLL)

Late Lumen Loss (㎜), Richard E. Kuntz et al., 1992, ISSN: 1524-4539

<Secondary efficacy endpoint>

■ Device success rate (N%)

During the procedure, when the distal part of the investigational device successfully reaches the target lesion and the balloon operates normally inflated and deflated and is recovered intact without rupture, the device is defined as successful, and the device success rate is evaluated.

■ Procedural success rate (N%)

In addition to success on coronary angiography[1)], it is defined as the absence of TLF (cardiac death, myocardial infarction attributable to target vessel (TV-MI), or ID-TLR) during hospitalization, and the success rate of the procedure is evaluated.

[1)] It is defined as a case where residual stenosis is less than 30% immediately after the treatment of the target lesion, blood flow is normal, and vascular dissection is confirmed to a degree that does not impede blood flow. At this time, residual stenosis is evaluated through coronary angiography images.

■ Restenosis rate (%) at 6 month after procedure

When a successfully treated lesion is evaluated through coronary angiography, restenosis is defined as a diameter stenosis(DS)** compared to the reference vessel diameter of 50% or more, and is evaluated at 6 months after the procedure. At this time, stenosis rate(DS,%) is evaluated through coronary angiography images.

** Definition of stenosis rate (DS, %) = (1-[MLD/RVD]) X 100

① Definition of in-lesion MLD(minimal lumen diameter, mm)

: It is defined as the diameter of the narrowest blood vessel measured through coronary

angiography.

② RVD (Reference vessel diameter, mm)

: It is defined as the average obtained by measuring the distal and proximal diameters of a certain section of the normal part of the blood vessel with the target lesion.

■ Target vessel failure(TVF) incidence rate (%) at 6 months after the procedure

TVF evaluates incidence rates.

TVF Definition: Composite of Cardiac Death, TV-MI, or ID-TVR

11.2. Safety evaluation

11.2.1. Safety evaluation variable

■ Adverse events

■ MACE(Major Adverse Cardiac Event) at 6 months after the procedure

11.2.2. Safety evaluation criteria and methods

■ Adverse events

In this clinical trial, adverse events are classified into adverse events that occurred before the application of the investigational device and adverse events that occurred after the application of the investigational device (Treatment Emergent Adverse Event, TEAE). (The definition and evaluation of adverse events is referred to '15. Evaluation criteria, evaluation methods, and reporting methods for safety, including side effects' section.) Adverse events that occurred before application of investigational devices are recorded as adverse events before treatment, but are excluded from adverse event analysis. In other words, adverse event analysis targets TEAEs.

All adverse events that occur are standardized into SOC (System Organ Class) and PT (Preferred Term) using the latest version of MedDRA (Medical Dictionary for Regulatory Activities).

■ MACE(Major Adverse Cardiac Event) 6 months after the procedure

① Cardiac death

: Death of unknown cause is classified as cardiac, and according to the definition of ARC, Composite endpoint of cardiac death (CEC) indicates the possibility of restenosis of the target lesion, and death accompanied by thrombosis of the target lesion is determined to be the cause of cardiac death.

② Whether myocardial infarction(MI) occurred or not

: It is evaluated as ST-segment elevation myocardial infarction and non-ST-segment elevation myocardial infarction.

ST-segment elevation myocardial infarction: When there is persistent chest pain for more than 30 minutes, the CK-MB fraction increases to more than three times the normal level, and the ST segment is elevated on an electrocardiogram.

Non-ST-segment elevation myocardial infarction: When the ST segment is not elevated on an electrocardiogram.

③ Whether Target vessel Thrombosis occurred or not

: According to the definition of ARC, it is classified and evaluated as follows.

- Certainty of diagnosis: definite/probable/possible
- Elapsed time: Early (0-30 days)/Late (31-180 days) from interventional surgery

④ Whether revascularization is performed: ID-TLR, TVR

- ID-TLR(Ischemia-Driven Target Lesion Revascularization) is a percutaneous intervention for the target lesion if the treated target lesion has an internal diameter stenosis of more than 50% and symptoms of angina pectoris, myocardial ischemia is suspected in an objective test, or both exist. Defined as one case.
- TVR (Target Vessel Revascularization) is defined as any percutaneous intervention or coronary artery bypass surgery performed on the treated target vessel.

12. DATA COLLECTION AND STATISTICAL ANALYSIS

12.1. General considerations

In the case of continuous data, the number of observed subjects, mean, standard deviation, median, minimum and maximum values are presented by applicable group, and in the case of categorical data, the frequency and ratio by applicable group are presented. Figures with values below decimal points, such as mean, standard deviation, and percentage, are rounded off to 3 decimal places and presented up to 2 decimal places.

12.2. Definition of evaluation analysis group

12.2.1. Effectiveness evaluation analysis group

■ FA set (Full Analysis Set)

It is defined as all subjects who received investigational devices in this clinical trial.

■ PP set (Per Protocol Set)

Among the subjects included in the FA set, it is defined as all subjects who completed the clinical trial without violating the clinical trial protocol. However, if dropouts and/or serious violations of

the clinical trial protocol do not affect the efficacy evaluation, they may be included in the PP set.

Protocol violation matters

- When a violation of the selection/exclusion criteria is discovered
- When investigational devices are not applied according to the prescribed method
- Other cases that may be considered serious violations of the clinical trial protocol

Effectiveness analysis is performed for each of the FA set and PP set, and if the subjects included in the analysis group are different, all results are presented. The final effectiveness evaluation is based on the PP set results.

12.2.2 Safety evaluation analysis group

■ Safety set

It is defined as all subjects who received investigational devices in this clinical trial.

12.2.3 Handling of missing data (missing values)

In case of missingness in the efficacy evaluation variables of this clinical trial, it is replaced by the method below. In case of missing items for other items, no replacement is made.

< Primary efficacy endpoint : in-lesion late lumen loss (mm) at 6 months after the procedure>

1) If omission occurs after PCI at 6 months, the subject is not treated as a dropout and is replaced on the assumption that the dilated vessel diameter (MLD, mm) immediately after the procedure will have decreased after the follow-up period (6 months).
2) In case of missing information due to dropout, it is replaced by assuming that the dilated vessel diameter (MLD, mm) immediately after the procedure has decreased after the follow-up period (6 months). However, if a patient drops out due to pregnancy after the procedure, they are excluded from the analysis without replacement.

< Secondary effectiveness endpoint>

1) If there is an omission in the device success rate and procedure success rate among the secondary effectiveness evaluation variables, it is replaced with 'failure' for analysis.
2) If there is an omission in the restenosis rate at 6 months after the procedure, it is replaced with the occurrence of restenosis. However, if a patient drops out due to pregnancy after the procedure, they are excluded from the analysis without replacement.

※ *Missing value processing is applied to the FAS group.*

■ Statistical analysis method

This study is a pilot study to check the mean, standard deviation, median, minimum, and maximum of the test group, and the purpose of this study is to calculate the sample size for this study in

the future.

13. STANDARDS AND HANDLING METHODS FOR CLINICAL TRIAL SUSPENSION AND WITHDRAWAL

13.1. Standards for clinical trial suspension and withdrawal

① In cases where it is difficult to continue the clinical trial due to adverse events, disease outbreaks, etc., according to the judgment of the investigator.
② Withdrawal of consent by the subject or the subject's representative
③ When follow-up observation of the subject is impossible
④ If target lesion revascularization was performed before the first efficacy evaluation
⑤ In cases where drugs and non-drug treatments (including procedures and surgery) that may affect the safety and effectiveness evaluation other than target lesion recanalization are concurrently or necessary
⑥ If the investigational device is not applied according to the procedure
⑦ If a violation of the selection/exclusion criteria is discovered during the clinical trial period
⑧ If pregnant
⑨ If the subject does not comply with the investigator's instructions or does not comply with the matters presented in the subject explanation and consent form
⑩ Other cases where the test manager determines that it is difficult to continue the clinical trial

13.2. Handling method for clinical trial suspension and withdrawal

■ Processing of withdrawal of clinical trial participation
① Appropriate treatment or treatment will be administered to subjects who have stopped participating in clinical trials, as necessary, and their progress will be observed thereafter.
② The reason for suspension and data related to clinical trials conducted before suspension are recorded and stored in the case report form, and a written explanation for suspension is submitted to the Institutional review board.
③ Data from subjects who have been suspended can be included in the Safety set and FA set, and can be excluded from the PP set.

■ Dropout from clinical trial
① The reasons for withdrawal and data related to clinical trials conducted before withdrawal are recorded and stored in the case report form, and a written reason for withdrawal is submitted to the Institutional review board.
② If follow-up observation of the subject is impossible, every effort must be made to confirm the subject's residence and health status.

③ Data from subjects who have been eliminated can be included in the Safety set and FA set, and can be excluded from the PP set.

13.3. Clinical trial suspension and early termination

If any of the following situations or events occur while this clinical trial is in progress, the principal investigator and sponsor may terminate or suspend this clinical trial early after appropriate discussion, but are not limited to this.

① When a clear or unacceptable risk is discovered for the subjects registered in this clinical trial

13.4. Processing of clinical trial suspension and early termination

① If a clinical trial is terminated or suspended early without prior agreement with the sponsor, the principal investigator must immediately notify the sponsor and the review committee of this fact and submit a detailed written explanation for the early termination or suspension.
② If a clinical trial is terminated or suspended early, the principal investigator must immediately notify the review committee of this fact and submit a detailed written explanation for the early termination or suspension.
③ If the review committee terminates or suspends a clinical trial early, the principal investigator must immediately notify the sponsor of this fact, and the head of the testing institution must immediately notify the Minister of Food and Drug Safety and submit a detailed written explanation for the early termination or suspension.
④ If the relevant clinical trial is terminated or stopped early in accordance with the provisions of ① to ③, the principal investigator must immediately notify the subject of this fact and ensure that appropriate measures and follow-up investigations are carried out.
⑤ Data related to clinical trials conducted until suspension are recorded and stored in the case report form.

14. SAFETY EVALUATION CRITERIA, EVALUATION METHODS, AND REPORTING METHODS, INCLUDING SIDE EFFECTS

14.1. Definition of adverse event

① "Adverse Event (AE)" refers to any unintended signs (including abnormalities in laboratory test results, etc.), symptoms, or diseases that occur in subjects during clinical trials. It does not necessarily have to have a causality with the relevant investigational device.

② "Adverse Device Effect (ADE)" refers to any harmful and unintended reaction caused by a investigational device, where the causality with the investigational device cannot be denied.
③ "Unexpected Adverse Device Effect" refers to differences in the pattern or degree of harm of an adverse device effect in light of available medical device-related information, such as the clinical investigator data sheet or medical device attachment documents.

14.2. Definition of serious adverse events and adverse device effect

"Serious AE/ADE" refers to any of the following cases among adverse events or adverse device effect caused by medical devices used in clinical trials.

① In case of death or danger to life
② When there is a need to be hospitalized or to extend the hospitalization period
③ In case of permanent or serious disability or decline in function
④ If a deformity or abnormality occurs in the fetus
⑤ Other medically important cases

14.3. Evaluation criteria and records of adverse events

The investigator evaluates and classifies all adverse events that occurred during the clinical trial according to the following guidelines and definitions and records them in the case report form.

14.3.1. Severity Assessment

When an adverse event occurs, the severity of the adverse event is evaluated according to the following criteria.

① Mild
When it does not interfere with the subject's normal daily life (function), causes minimal discomfort, and is easily tolerated by the subject.

② Moderate
If it causes inconvenience that significantly impairs the subject's normal daily life (function)

③ Severe
When it makes the subject's normal daily life (function) impossible

14.3.2. causality assessment with investigational devices

The relevance to investigational devices is assessed in accordance with the evaluation criteria in Article 7, Review and Evaluation of Adverse Events, Paragraph 2 [Appendix 3] of the Regulations on Safety Information Management, including Side Effects of Medical Devices, and the investigator's opinion is described.

Causality	Assessment criteria
Definitely related	• The relationship between the occurrence of adverse events and the use of medical devices is reasonable, and is most likely to be explained by the use of medical devices rather than other reasons. If the symptoms of an adverse event that occurred due to discontinuation of use of the medical device disappear, and symptoms of the adverse event appear when it is reused (only when reuse is possible) • Additionally, if the adverse event that occurred is consistent with information already known about the relevant medical device or medical devices of the same series.
Probably related	• There is evidence of use of the medical device, the temporal sequence of use of the medical device and occurrence of the adverse event is reasonable, it is more plausibly explained by the use of the medical device than other causes, and it occurred due to discontinuation of use of the medical device. When the symptoms of an adverse event disappear
Possibly related	• There is evidence of use of the medical device, the temporal sequence of use of the medical device and occurrence of the adverse event is reasonable, it is judged to be attributable to the use of the medical device to the same extent as other possible causes. When the symptoms of an adverse event that occurred due to discontinuation of use disappear.
Possibly not related	• If there is evidence of use of the medical device, there is a more likely cause for the adverse event, and the symptoms of the adverse event that occurred after discontinuation of use of the medical device disappear or are ambiguous. • And when the medical device is reused (only when reuse is possible) and the results do not show symptoms of an adverse event or are ambiguous.
Definitely not related	• If the relevant medical device was not used, or the temporal sequence between use of the relevant medical device and occurrence of adverse events is not reasonable. • When there is another obvious cause for an adverse event
Unknown	• When the information is insufficient or conflicting and a decision cannot be made and cannot be supplemented or confirmed.

14.3.3 Measures for investigational devices

Since the medical devices for clinical trials in this clinical trial are applied only once and do not remain in the body, there is no application for measures against investigational devices.

14.3.4 Treatment content and results

Treatment and results of adverse events are recorded according to the following classifications.

- Treatment details
  - No treatment
  - Drug administration
  - Procedures and surgeries
  - Other

- Result
  - Recovery, no after-effects
  - Recovery, after-effects
  - Recovering
  - No recovery
  - Death
  - Unknown

14.4. Suspected adverse events

The following adverse events may occur, and signs, symptoms, or diseases other than those listed may also occur.

<Adverse cases related to coronary intervention>

- Acute myocardial infarction
- Allergic reaction
- Aneurysm or pseudoaneurysm
- Rupture of coronary artery
- Arrhythmias including ventricular fibrillation(VF) and ventricular tachycardia(VT)
- Cardiac tamponade or pericardial effusion
- Cardiogenic shock / pulmonary edema
- Coronary artery spasm(CAS,)
- Death
- Fever
- Heart failure
- Hematoma

- Bleeding/bleeding requiring blood transfusion
- Low blood pressure / high blood pressure
- Localized or systemic infection
- Inflammation
- Vascular occlusion
- Pain or tenderness at access site
- Renal failure
- Stroke, Cerebrovascular disorder / Transient ischemic attack (TIA)
- Systemic embolic occlusion
- Thrombosis

<Adverse cases related to drug(paclitaxel)>

- Allergy / immune response
- Alopecia
- Anemia
- Blood transfusion
- Digestive system symptoms
- Blood diseases(leukopenia, neutropenia, thrombocytopenia)
- Liver enzyme alterations
- Modification of blood vessel wall tissue, including infection, cell damage, or necrosis
- Muscle pain/joint pain
- Peripheral neuropathy
- Cardiac conduction abnormalities
- Pseudomembranous colitis

14.4.1 How to check and respond to suspected adverse events

The occurrence of suspected adverse events is monitored through physical examination, vital signs, and coronary angiography during the follow-up period. If an adverse event is confirmed or suspected, the investigator treats the adverse event through procedures or drug administration or conducts additional tests. can be implemented. For details on how to evaluate and respond to expected adverse events, follow the institution's standard procedures.

14.5. How to report adverse events

14.5.1. Adverse events reporting training

The principal investigator should inform the sub-investigator, subjects, or representative of all adverse events that may occur after surgery or use of investigational devices and provides training to report through the reporting system and specified deadlines and reporting forms described in the '15.5.3. Reporting of serious adverse events/adverse device effects' section.

14.5.2. Records of adverse events

When an adverse event occurs, the investigator records the following information in the case report form.

- Name of adverse event
- Start and end dates
- Severity
- Causality with medical devices for clinical trials
- Treatment content and results

14.5.3 Serious adverse event/adverse device effects reporting

The person in charge of the study shall immediately report to the principal investigator after recognizing any serious adverse events/adverse device effects that occurred during the clinical trial period. The principal investigator records reported serious adverse events/adverse device effects in the serious adverse event record, and must be reported to the sponsor within 24 hours as an adverse device effects rapid report according to Form No. 55 of the Enforcement Rules of the Medical Device Act, regardless of whether it is related to a medical device for clinical trials. (However, serious adverse events/adverse device effects presented in '15.4. Expected adverse events' of the clinical trial protocol do not need to be reported within 24 hours.) At this time, in order to protect the confidentiality of the subject's personal information, the principal investigator must use the subject identification code in place of the subject's personal information such as the subject's name, resident registration number, and address. If there are guidelines for reporting adverse events, follow these. Must follow.

In addition, events that are considered serious by the principal investigator or that suggest significant risks, contraindications, side effects, or cautions that may be associated with the use of medical devices for clinical trials are recorded as serious adverse events/adverse device effects and reported immediately.

When reporting a case of death, the principal investigator must submit additional information, such as an autopsy report (only applicable to cases where an autopsy was performed) and a death certificate, to the sponsor and the Institutional Review Board.

The sponsor shall report all serious and unexpected adverse device effects to the investigator, the review board (applicable only in cases where the principal investigator did not report to the review board or there is a need to change the reported matters), and the Minister of Food and Drug Safety in the deadline of following categories.

① If it causes death or threatens life, the sponsor must report the adverse device events within 7 days from the date the sponsor received the report or became aware of this fact. In this case, the sponsor must additionally report detailed information on the adverse device

effects within 8 days from the date of initial report. do.

② In case of any other serious and unexpected adverse device effects, they must be reported within 15 days from the date the sponsor receives or becomes aware of this fact.

If there is additional information about the adverse device effects reported in accordance with ① and ②, the sponsor must report it until the adverse device effects are terminated (refers to when the adverse device effect disappears or follow-up investigation becomes impossible).

If the sponsor wishes to report an adverse device effect to the Minister of Food and Drug Safety in accordance with ① and ②, the adverse device effects report according to Form No. 56 of the Enforcement Rules of the Medical Device Act and the appendix reported by the principal investigator in accordance with the relevant laws and regulations. A rapid report on adverse device effects according to Form No. 55 must be attached and submitted.

15. MEAUSURES FOR THE SAFETY PROTECTION OF SUBJECTS

15.1. Korean good clinical practice(KGCP) and declaration of Helsinki

The procedures prescribed in this plan were prepared for the test sponsor and clinical trial investigators to comply with the basic spirit of the ICH-GCP and the Declaration of Helsinki in conducting, evaluating, and recording results of this trial. This clinical trial will also be conducted in accordance with national regulations (medical device clinical trial management standards.

15.2. Institutional review board(IRB)

IRB shall examine whether the PI has the appropriate experience and qualifications to conduct the relevant clinical trial based on the history and other experience of the PI. A review shall be conducted at least once a year for the clinical trial being conducted, and the review cycle shall be determined according to the degree of risk that may pose to the subject.

IRB may request the head of the clinical trial institution or the test director to suspend the clinical trial if the clinical trial being conducted is conducted differently from the requirements or decisions of the review committee or if an unexpected serious risk occurs to the subject.

If it is deemed necessary to protect the rights, safety, and welfare of the subject, the Review Committee may request the sponsor to provide additional information to the subject other than information pursuant to subparagraph 10 of Item 7 of the Enforcement Rules of the Medical Device Act "[Attachment 3] Medical Device Clinical Trial Management Standards.

If the subject receives financial compensation in exchange for participating in the clinical trial,

the judging committee shall examine the amount of compensation, the method of compensation, and whether the financial compensation unreasonably affects the subject's participation in the clinical trial. In this case, it shall be reviewed whether the financial compensation is appropriate in light of the subject's degree of participation in the clinical trial and the period of participation, and whether the compensation for the subject is conditional on participation in the clinical trial until the end. In addition, it shall be confirmed whether information on financial compensation, such as the payment method, amount, and payment time, is clearly recorded in the subject's manual or other documents provided to the subjects, and the judging committee shall confirm whether there is a compensation plan for the subjects who have not completed the clinical trial.

15.3. Informed consent form

Written consent must be received from each subject (or the subject's representative) before screening evaluation for clinical trials is conducted. The investigator shall give the subject (or the subject's representative) sufficient time to explain in detail all matters related to the clinical trial and to know about all predictable results for those who have met all the selection/exclusion criteria before starting the clinical trial. A signed copy of the consent shall be kept by the subject and the original copy shall be kept by the investigator.
The investigator shall prepare and keep a list of all subjects who have agreed to participate in the clinical trial and submit it to the clinical trial sponsor upon request.
Subjects should be informed of the fact that the subject's clinical trial-related data will be used by the sponsor and the level of disclosure in accordance with the medical device clinical trial management standards. In addition, the subject should be informed that the subject's medical records can be reviewed by the clinical trial monitoring personnel or the person conducting the inspection, the IRB, and the head of the Ministry of Food and Drug Safety.

If the clinical trial plan is revised, the subject's explanation and consent form may be revised to reflect the changes in the clinical trial plan. If the subject's explanation and consent form are revised, it must be reviewed and approved by the IRB, and the newly registered and currently participating subjects must explain the changes and obtain signature on the revised consent form.

☞ *Annex _ Refer to the subject's explanation and consent form*

15.4. Protocol of Subject Compensation

If the subject is damaged by clinical trial medical device use or clinical procedures that he or she would not have received if he or she did not participate in this clinical trial, all treatment will be performed in accordance with the standard procedures of the hospital, and if any injuries occur due to this clinical trial, compensation will be made in accordance with the victim compensation agreement and the clinical trial insurance policy terms and conditions signed up by the sponsor.

☞ *Annex _ Refer to the Victim's Compensation Code*

15.5. Measures for Safety Protection of Subject

If new information is obtained that may affect the continuation of this clinical trial, the information will be provided to the subject (or the subject's representative) in a timely manner, and the investigator will discuss with the subject whether to continue participation in the clinical trial.

15.6. Subject's medical treatment and treatment criteria after clinical trial

If the subject drops out of the clinical trial due to adverse event or has residual symptoms due to side effects and adverse event after completion of the clinical trial, he/she will receive sufficient treatment in accordance with the hospital's standard medical guidelines until he/she recovers by performing appropriate medical measures such as drug administration and procedures for the adverse event. Subjects who have completed the clinical trial without adverse event will undergo general clinical observation according to the hospital's standard procedures after the clinical trial. In the event of any injuries caused by this clinical trial, the cost will be compensated according to the Victim Compensation Covenant and the clinical trial insurance policy signed up by the sponsor.

15.7. Clinical trial center

The head of a clinical trial institution shall be equipped with clinical laboratories, facilities, and specialized personnel necessary for conducting the relevant clinical trial, and shall ensure that the relevant clinical trial can be properly conducted, such as taking necessary measures in case of emergency.

15.8. Investigator

The definition and obligations of the investigator are as follows.

① The term "investigator" refers to the principle investigator, investigator, and coordinating investigator. The investigator shall conduct clinical trials in compliance with the clinical trial plan agreed with the sponsor and approved by the IRB and the Minister of Food and Drug Safety.

② In accordance with "1.26. Report of serious Adverse event/ Adverse device effects", the principle investigator is obligated to recognize adverse event and report them to the principle investigator, and the principle investigator is obligated to report the adverse event reported from the principle investigator to the sponsor.

③ All medical decisions regarding clinical trials in subjects are made by a principal investigator or sub-investigator with the qualifications of a doctor, dentist, or oriental doctor.

④ During or after a clinical trial, the investigator shall ensure that the subject receives appropriate medical treatment for all abnormalities in the clinical trial (including abnormalities in the results of clinically meaningful laboratory tests), and shall inform the subject if the incidental disease of the subject, which the investigator has become aware of, requires medical treatment.

⑤ If the subject has an attending physician, the principle investigator may inform the attending physician of the subject's participation in the clinical trial with the consent of the subject.

⑥ The subject does not have to disclose the reason if he/she stops participating in the clinical trial before completion of the clinical trial, but the principle investigator shall endeavor to confirm the reason to the extent that it does not infringe on the subject's rights.

15.9. Sponsor of clinical trial

The obligations of the sponsor are as follows.

① The sponsor must have a person with knowledge and experience in clinical trials supervise the overall conduct of the clinical trial and be responsible for data processing and verification, statistical analysis, and preparation of result reports.

② The sponsor may establish a data monitoring committee to periodically evaluate the progress of the clinical trial, including safety-related data and important efficacy outcome variables, and advise on whether to proceed, change, or stop the clinical trial. The data monitoring committee shall Standard work instructions necessary for work performance must be prepared, and meeting minutes must be prepared and stored.

③ The sponsor must prepare compensation procedures for damages incurred in connection with the clinical trial.

④ Compensation for subjects must be appropriately made in accordance with the content and method of compensation stipulated in relevant regulations and relevant laws and regulations.

⑤ In the case of a multi-center clinical trial, the sponsor must determine whether all principal investigators are conducting the clinical trial in accordance with the clinical trial protocol agreed upon with the sponsor and approved by the IRB the Minister of Food and Drug Safety, and whether all principal investigators are complying with the clinical trial protocol; It should be checked whether communication between investigators is smooth.

16. OTHER MATTERS NECESSARY TO CONDUCT

CLINICAL TRIALS SAFELY AND SCIENTIFICALLY

16.1. Confidentiality

16.1.1. Data

The investigator comply with the confidentiality of all information related to the clinical trial plan provided by the sponsor or clinical trial monitoring agent. However, exceptions are made when the IRB, the subject, or the Ministry of Food and Drug Safety requests disclosure in accordance with laws or related regulations.

16.1.2. Privacy policy and anonymity of subjects

The anonymity of the subjects participating in the clinical trial must be guaranteed. The identification of the subject should be made with the subject identification code. The subject is informed that all clinical trial data are strictly confidential. The original signed subject's explanation and consent form shall be kept by the principal investigator. The principal investigator shall have a list of subject identification codes and subject names recorded and, if necessary, records may be found. The subject's explanation and consent form and subject list shall be kept in the clinical trial institution for 3 years after the end of the clinical trial (However, in the case of a clinical trial for manufacturing permission, import permission, or change permission, data shall be kept for 3 years after the date of permission).

At this time, the data for subject identification must be strictly confidential by the investigator. However, exceptions are made when necessary to be audited by health authorities, clinical trial monitoring personnel, sponsor, or designated agents, and the investigator must provide the information after fully understanding the confidentiality of the information.

16.2. Compliance and modification of protocol

Neither the principle investigator nor the sponsor may change the contents of this clinical trial plan without the consent of the other party. All changes to the clinical trial plan must be discussed with the sponsor, and the clinical trial change plan is prepared by the sponsor. When changing the plan, the date of revision, the reason for revision, the details of the revision, etc. must be recorded, and all relevant parties must sign and agree in writing.

If a previously approved clinical trial is to be changed and carried out, the change plan shall be approved by the examination committee of the relevant testing agency and the Minister of Food and Drug Safety (if it falls under the following items).

① If there is a risk of causing new safety and effectiveness problems due to changes in

technical characteristics such as the structure and principle of the medical device for clinical trials

② Development plan to change or add the purpose of use

③ Manufacturing plant of clinical trial medical device to be used

④ a clinical trial institution

⑤ Number of subjects participating in clinical trials, criteria for selection and exclusion of subjects, etc.

⑥ Evaluation of safety and effectiveness of clinical trial medical devices or observation items directly related to the subject's safety, observation period, etc.

⑦ Other cases where the Minister of Food and Drug Safety deems it necessary

Minor modifications or specifications that do not affect clinical trials (if they do not fall under the above items) do not necessarily require approval from the Ministry of Food and Drug Safety and require administrative changes.

The investigator shall not apply these changes to the clinical trial plan until approval for review is obtained from the Ministry of Food and Drug Safety and the IRB. Serious violations of the clinical trial plan shall be recorded in the case report form. However, in only the following cases, clinical trials may be conducted differently from the test plan before obtaining approval for the changed plan.

1) Immediate risk factors that have occurred to the subject need to be removed

2) Where matters related to administrative procedures, such as changes in monitoring personnel, changes in test personnel, changes in emergency contact telephone numbers, etc., are to be changed

The principal investigator shall submit a document containing the facts and reasons for implementation of the change plan to the sponsor, the examination committee of the testing agency and the head of the Ministry of Food and Drug Safety as soon as possible for changes made without prior approval from the review board for the removal of immediate risk factors that have occurred to the subject for agreement and approval.

16.3. Clinical trial monitoring

16.3.1. Process of clinical trial monitoring

Prior to the start of the clinical trial, the sponsor, the principal investigator, and the person in charge of the clinical trial trustee will hold a research meeting or a clinical trial initiation meeting for this clinical trial. In this meeting, detailed discussions on clinical trial plans, clinical trial procedures, case report form, and test methods will be held. Investigator who cannot attend these meetings or meetings, or who will participate in the clinical trial later, should receive appropriate training by the sponsor, the principal investigator, or the person entrusted to them.

The sponsor shall appropriately provide relevant guidelines and data to the clinical trial institution, designate a monitoring agent to be in charge of this clinical trial, and visit and monitor the clinical trial institution before the start of the clinical trial and during the clinical trial period. Monitoring and audit can be conducted by the clinical trial sponsor in order for clinical trials to be conducted in accordance with the medical device clinical trial management standards and for clinical trial data to be recognized when registered at home and abroad.

16.3.2. Duty of clinical research associate

The clinical research associate (CRA) explains the monitoring plan to the examiner before starting the clinical trial, and during the monitoring visit, the examiner checks whether the clinical trial is carried out in accordance with the clinical trial plan and related regulations. The clinical trial monitoring agent is approved to visit and contact the examiner on a daily basis and monitor various records of the clinical trial.
It is the responsibility of the clinical trial monitoring personnel to regularly monitor case report form throughout the clinical trial period to prove the completeness, consistency and accuracy of the recorded data and to prove that the recorded data were faithful to the clinical trial plan. Discussions should be made with the sponsor or investigator appropriately. The investigator shall appropriately inform the clinical trial monitoring personnel of any findings during the clinical trial and cooperate in monitoring activities.

16.4. Record and use of test results

16.4.1. Case report form and source document

In this clinical trial, data are collected using a paper CRF (or electronic case report form, eCRF) in the form of a paper document.

The investigator shall ensure that the case report form reported to the sponsor or the data contained in all other reports are accurate, complete, readable, and timely. After preparing the case report form, the investigator shall ensure that the information recorded in the case report form is true by signing each case report form. In all cases, the investigator shall have final responsibility for the accuracy and reliability of all clinical and laboratory test results recorded in the case report form.

The data on the case report form based on the supporting document shall match the supporting document, and explanations shall be attached to the inconsistent content.

The investigator shall allow direct access to the supporting data and supporting documents during monitoring, inspection, review by the clinical trial review committee, and due diligence related to the clinical trial. Each subject's original case report form will be confirmed by the clinical trial monitoring staff by comparing it with the supporting documents at the clinical trial

institution. Anyone who changes or corrects the contents of paper CRF or eCRF shall modify and write the reason for the correction so that the original contents can be identified according to the correction guidelines prepared by the sponsor. At this time, the date of correction and signature must be additionally written on the paper CRF.

Evidence documents, case report forms, and other clinical trial-related documents should be kept in a clinical trial institution. In the case of paper CRF, the sponsor recovers the original copy after the clinical trial is completed and keeps a copy in the clinical trial institution. The investigator shall keep all records related to the clinical trial until the legally determined deadline, and then until the deadline determined by the sponsor.

16.4.2. Storage of clinical data

All case report forms and related data and management records shall be kept by the clinical trial sponsor and the head of the clinical trial institution for three years after the end of the clinical trial (but, in the case of a clinical trial for manufacturing permission, import permission, or change permission, data shall be kept for three years after the date of permission). No clinical trial data shall be destroyed or moved to another place without the prior written consent of the sponsor. If the investigator is excluded from the clinical trial due to relocation, retirement or other reasons, the sponsor shall be informed and an appropriate solution shall be agreed upon.

16.4.3. Use of clinical trial results

By signing this clinical trial protocol, the investigator agrees to use the results of this clinical trial for purposes such as registration, presentation, and provision of information to medical device experts.

After the clinical trial is completed, the principal investigator reviews all results, analysis data, and reports to develop an updated strategy for publication. All publications must be prepared by the researcher.

16.5. Agreement between sponsor and head of clinical trial center

The sponsor's obligations when signing a principal investigator contract are as follows.

① The sponsor shall enter into a clinical trial contract with the head of the clinical trial institution as a document, and may, if he/she intends to conduct a multi-center clinical trial, make a comprehensive contract with the head of one clinical trial institution.

② The contract shall include matters concerning the finance of clinical trials, such as the size and method of payment of research funds, the return of unused research funds upon early termination and the suspension of clinical trials, matters concerning the delegation and division of duties, and obligations of the sponsor and the head of the clinical trial institution.

16.6. History of Principal investigator

The history of the Investigator shall be as follows.

In order to properly conduct clinical trials, investigators must have the education, training, and experience necessary to conduct clinical trials in accordance with the standard operating instructions of clinical trial institutions. Investigators must have detailed knowledge of the appropriate use of clinical investigational medical devices as specified in the clinical trial protocol, clinical investigator brochure, and other medical device-related information. Investigators must closely understand and comply with relevant laws and regulations.
If important clinical trial-related tasks are delegated to a study manager, the study director must secure and maintain a list of study personnel.
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16.7. Use and management of Investigational device

Medical devices for clinical trials are managed by a person designated by the head of the relevant clinical trial institution or a medical device manager designated by the trial director with the approval of the clinical trial institution. Medical device managers are responsible for managing medical devices for clinical trials. Medical devices for clinical trial use must be handled and stored as described in the description and include the phrase "for clinical trial use." The manager of medical devices for clinical trials must perform tasks such as acquisition, inventory management, and return of medical devices used in clinical trials, maintain related records, and periodically notify the study director of such matters. Related records must include the application period, manufacturing number or serial number, medical device identification code, and clinical trial subject identification code of the clinical trial medical device for each clinical trial subject. In addition, medical records must be maintained to confirm whether medical devices for clinical trials have been used according to the usage instructions specified in the clinical trial protocol for each clinical trial subject, and it must be checked whether the inventory of medical devices for clinical trials matches the usage records.

16.8. Supply and handling of Investigational device

The principal investigator shall not supply medical devices for clinical trials to managers, etc. before obtaining approval from the IRB and the Minister of Food and Drug Safety for the clinical trial protocol.

Investigators must have documented procedures for how managers, etc., handle and store clinical trial medical devices, which include appropriate and safe receipt, handling, storage, return of unused clinical trial medical devices from clinical trial subjects, and Methods for returning it to the person in charge of research are included.

Medical devices for clinical trials must be supplied in a timely manner, and records must be maintained regarding supply to the clinical trial institution, acquisition by the clinical trial institution, return from the clinical trial institution, and disposal.

Investigators must establish and document a recall system for medical devices for clinical trials when problems such as malfunctions occur with the medical devices for clinical trials, or when clinical trials are completed or expiration of the period of use.

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Protocol Agreement

Clinical trial title	A Small scale, Prospective, Multicenter, Single arm, Investigator-Initiated Feasibility Clinical Study to Evaluate the Efficacy and Safety of Paclitaxel Coated PTCA Balloon Catheter (GENOSS® DCB) in Patients with De novo lesion of coronary artery
Protocol No.	CEP-DS1001_FS

Principal investigator/ Coordinating investigator

I have read and reviewed this clinical trial protocol, understand it in its entirety, and agree to proceed with the clinical trial in accordance with it. I will conduct this clinical trial in accordance with the ICH-GCP (International Council of Harmonization-Good Clinical Practice) standards and all related regulations, and will fulfill my duties as a principal investigator in accordance with the Declaration of Helsinki and the ethical standards of the Institutional Review Board.

_____

Clinical trial institution name

_____	_____	_____
Principal investigator name	Signature	Date (YYYY-MM-DD)

Protocol Agreement

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Principal investigator name	Signature	Date (YYYY-MM-DD)