Protocol for Post-Marketing Surveillance

GORE® VIABAHN® Endoprosthesis Post-Marketing Surveillance Study - Treatment of patients with stenosis or occlusion at the venous anastomosis of synthetic arteriovenous (AV) access graft

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1 Medical device for surveillance

Category	Instrument and Apparatus(07)Visceral Function Substitute Device
Generic name	Stent graft with heparin for central circular system (Vascular stent graft with heparin)
Brand name	GORE® VIABAHN® stent graft

2 Purpose

To confirm the efficacy and safety in the clinical setting after the launch of the GORE® VIABAHN® stent graft (hereafter referred to as "Viabahn") for the treatment of patients with stenosis or occlusion at the venous anastomosis of synthetic arteriovenous access graft

3 Target number of cases and rationale for setting

Target number of cases：100 cases（indicated cases）

Rationale：

[redacted]

4 Target patients

Patients who developed stenosis or occlusion at the venous anastomosis of synthetic arteriovenous access graft (indicated cases) will be target patients. In addition, patients

who was used to repair vascular access circuits for purposes other than treatment of stenosis or occlusion at the venous anastomosis of synthetic arteriovenous access graft will be also enrolled in this surveillance and this surveillance will be conducted in conjunction with the indicated cases.

5 Planned sites

After the start of this surveillance, the sites which concluded a contract based on the standards for Good Post-marketing Study Practice (hereafter referred to as "GPSP ordinances ") and used Viabahn, and in addition to that, the sites which have physicians determined to be able to use Viabahn properly will be the planned sites. The number of sites by departments where this surveillance may be conducted is as follows. During this surveillance, the number of sites may vary depending on the enrollment status.

Clinical departments	Planned number of sites
Urology	1
Nephrology	6
Cardiology	1
Surgery	3
Dialysis	1
Vascular surgery	1

In this surveillance, it is important to collect treatment results by physicians in clinical departments performing dialysis who have not previously used Viabahn, and assess the sufficiency of the post-marketing safety measures. Therefore, sites should be chosen so that patients are enrolled in a fixed number even in clinical departments where dialysis is performed.

The AVR 06-01 study conducted in the United States was conducted at 31 sites, and 289 subjects were enrolled (143 in Viabahn group and 146 in PTA group).

6 Method of surveillance

This surveillance complies with Act on Securing Quality, Efficacy and Safety of Products Including Pharmaceuticals and Medical Devices and GPSP ordinances and uses Electronic Data Capture systems (hereafter referred to as "EDC") to collect information on cases who used Viabahn after concluding a contract in the sites.

This surveillance will be conducted with a consecutive surveillance system in which patients who used Viabahn are enrolled consecutively in this surveillance. Inclusion, enrollment, data bases for analysis will be prepared according to the following procedures.

(1) Enrollment should be performed after fully explaining the purpose and plan of this surveillance and concluding a contract with sites for this surveillance. Enrollment is completed by providing case information on the Case Registration Form from site staff to the contract research organization (hereafter referred to as "CRO") and receiving it by CRO.
(2) After obtaining the information on the Case Registration Form, the CRO will make the data of the case available for entry into the EDC. The enrollment of the case will be completed by the fact that data can be entered into the EDC.
(3) When EDC becomes available for entry, investigator is asked to enter the surveillance information into the EDC, and the investigator or site staff enter the information into the EDC.
(4) Using the information entered in EDC, create a database for analysis.

7 Planned surveillance period

Total surveillance period：4 years after obtaining approval
Preparation period：about 8 months
Enrollment period：about 6 months
Follow-up period：24 months from procedure
Supplemental surveillance period, data fixed period, analysis period：about 10 months

8 Surveillance items, etc

8.1 Surveillance items

This surveillance collects following items. No focused survey items will be established in this surveillance.

(1) Treatment

- Patient information
  - Age, sex, height, weight, smoking history, family history of myocardial infarction, treatment history of ischemic heart disease, etc.
- Medical history
  - Myocardial infarction, transient ischemic attack, etc.
- Primary disease / Complication

- Primary disease : diabetic nephropathy, chronic glomerulonephritis, nephrosclerosis, polycystic kidney disease, chronic pyelonephritis, interstitial nephritis, rapidly progressive glomerulonephritis, nephritis associated with autoimmune diseases, etc.
- Complication : dyslipidemia, hypertension, diabetes mellitus, metabolic syndrome, heart failure, peripheral arterial disease, stroke, etc.

・ Pre-procedure information
- Echocardiography, electrocardiography, assessment of cardiac function, laboratory data (BNP, etc.), etc.

・ Characteristics of lesion
- Location of the lesion, palpation, auscultation, etc.

・ Secondary lesion information in the vascular access circuit after the procedure[1]

・ Procedure information at the time of treatment
- Procedure time, blood flow before and after the procedure[2], vein pressure[3], etc.

・ Information on Viabahn
- Item and Lot Number

・ Other device information used during treatment

(2) Follow-up information

・ Information on vascular access and Viabahn

・ Information on dialysis treatment continuation

・ Information on discontinuation

(3) Failure

・ Name of failure, date of occurrence, etc.

(4) Adverse events

・ Name of adverse event, date of onset, severity, causal relationship, etc.

(5) Re-treatment

・ Information on vascular access and lesions
- Blood flow and venous pressure before and after re-treatment, palpation,

[1] Lesions not treated with Viabahn at the treatment
[2] Refers to the blood flow through the entire shunt.
[3] Refers to static venous pressure (sVP) or dynamic venous pressure (dVP). The venous pressure should be measured by the same method before and after the initial placement and before and after re-treatment of each patient.

auscultation, etc.

- Information on re-treatment
  - Performed treatment, clinical indications, etc.
- Other device information used during re-treatment

(6) Concomitant drugs (antiplatelet drugs, etc.)

- Drug Name
- Date of first administration
- Date of completion of administration

8.2 Planned surveillance items at each visit

This surveillance will collect surveillance information at treatment, 1 month, 3 months, 6 months, 12 months, and 24 months. Planned surveillance items at each visit are as follows:

Table1 Planned surveillance items at each visit

	treatment	1 month	3 months	6 months	12 months	24 months
Patient information	X					
Medical history	X					
Primary disease/Complication	X					
Pre-procedure information	X					
Characteristics of lesion	X					
Secondary lesion information in the vascular access circuit after the procedure（the lesion not treated with Viabahn）	X					
Procedure information at the time of treatment	X					
Information on Viabahn	X					
Other device information used during re-treatment	X					
Follow-up information		X	X	X	X	X
Adverse events and failure	←----------	----------	----------	----------	----------	----------→
Re-treatment	←----------	----------	----------	----------	----------	----------→
Concomitant drugs (Antiplatelet drugs, etc.)	←----------	----------	----------	----------	----------	----------→

X: Input

8.3 Desired visit period

The desired visit period is as follows.

Table2 Desired visit period

Follow-up visit	Desirable visit period (days)
treatment	0
1 month	15 – 45
3 month	60 – 120
6 month	120 – 240
12 month	275 – 455
24 month	640 – 820

9 Items and methods for analysis

The following effectiveness and safety items will be evaluated.

9.1 Effectiveness endpoint

(1) Primary patency of target lesion

Primary patency of target lesion is defined as the period during the patency was maintained from initial treatment until occlusion[4] of target lesion or re-treatment[5] of target lesion. Primary patency of target lesions is calculated by Kaplan-Meier method.

(2) Secondary patency of target lesion

Secondary patency of target lesion is defined as the period during the patency was maintained from initial treatment (including the period of patency after re-treatment). Secondary patency of target lesions is calculated by Kaplan-Meier method.

(3) Primary patency of vascular access circuit

Primary patency of vascular access circuit is defined as the period during the patency was maintained from initial treatment until occlusion in vascular access or re-treatment in vascular access circuit. Primary patency of vascular access circuit is calculated by Kaplan-Meier method.

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[4] Occlusion lesions occurring in Viabahn or within 5mm from the periphery or center of Vaibahn

[5] Intervention for lesions (occlusion or stenosis) occurring in Viabahn or within 5mm from the periphery or center of Viabahn

(4) Secondary patency of vascular access circuit

Secondary patency of vascular access circuit is defined as the period during the patency was maintained from initial treatment until discontinuation of the use of vascular access circuit. Secondary patency of vascular access circuit is calculated by Kaplan-Meier method.

(5) Mean cumulative number of re-treatment in target lesion

Mean cumulative number of re-treatment in target lesion is defined as the number of re-treatment performed for target lesion after the initial treatment.

(6) Technical Success

Technical Success is defined as < 30% residual stenosis after initial treatment.
The residual stenosis should be calculated as follows.

$$\%\ \text{stenosis} = \frac{(\text{reference diameter} - \text{stenosis diameter})}{\text{reference diameter}} \times 100$$

The definition of stenosis diameter and reference diameter is as follows.
Stenosis diameter: Diameter of the thinnest part after deployment of Viabahn
Reference diameter: Diameter of the non-stenosis part in the vicinity of the stenosis

(7) Clinical Success

Clinical Success is defined as the resumption of normal dialysis for at least one session after the initial treatment.

9.2 **Safety endpoint**

(1) Incidence of device and procedure-related adverse events at treatment and up to 30 days after treatment.

(2) Incidence of adverse events and device defect in each follow-up period

The definitions of adverse events and failures in this surveillance are as follows.

Table3 Adverse events and failures in this surveillance

Adverse events	Any unfavorable or unintended sign (including abnormal laboratory changes), symptom, or illness associated with the use of a medical device. Unless worsening of severity or increasing of incidence during the surveillance, the primary disease of the patient is not considered an adverse event.
Device Defect	Defects such as damage, malfunction, etc. that are widely unfavorable. Regardless of whether they are due to design, marketing, distribution, or use. Medical device failures include the following: (1) Specification issues (2) Defective product (3) Malfunction or damage (4) Insufficient description of package inserts, etc. (5) Device-related adverse events

Serious adverse events are defined as any of the following adverse events.

(1) Death

(2) Disability

(3) Cases that may lead to death

(4) Cases that may lead to disability

(5) Requires hospitalization or prolongs an existing hospitalization

(6) Serious according to the cases listed in (1)~(5) above

(7) Any congenital disease or anomaly in the offspring of treated patient.

The term "hospitalization" in (5) does not include hospitalization (scheduled surgery, examination, etc.) intended only to carry out the scheduled therapy or examination before the surveillance during the surveillance period (however, any newly occurring during that hospitalization should be handled as an adverse event).

9.2.1 Collection period for adverse events and device defect

From the time of treatment to the end of the surveillance (24 months or discontinuation of the study). The time of treatment with Viabahn should be the time of initial treatment.

9.2.2 Evaluation of the causal relationship for adverse events

The causal relationship between the adverse event and surveillance device (Viabahn placed at the initial treatment) and procedure at initial treatment (placement of surveillance device) will be determined according to the table below, taking into account the condition of the patient, complications, medical history, and time-to-onset relationship. When necessary, the rationale for causal relationship assessment should be entered into the EDC.

Table4 Evaluation of the causal relationship for adverse events

Causal relationship	Criteria
No related to device or procedure	The surveillance device and procedure at initial treatment are not considered to be related to the adverse event.
Device-related	The surveillance device are considered to be related to the adverse event that occurred after the procedure at the initial treatment,
Procedure-related during placement of surveillance device	The procedure at the initial treatment is considered to be related to the adverse event
Unknown	The causal relationship between the surveillance device and the adverse event cannot be undeniable.

9.2.3 Evaluation of the outcome for adverse events

The outcome of adverse events will be assessed according to the table below.

Table5 Evaluation of the outcome for adverse events

Outcomes	Criteria
Recovery	In the case of disappearance / recovery of the adverse event and the adverse event related to laboratory values, normalization or recovery to values before placement level of the surveillance device
Remission	Reduced degree of the adverse event or with a tendency to improve
Not recovered	Little change in the extent of the adverse event or those with exacerbation
Death	Mortalities associated with the adverse event
Unknown	Undertaken the follow-up of the adverse event but have not been able to follow the outcome

10 Organizational structure for surveillance

Same as the basic plan for post-marketing surveillance.

11 Information of outsourcing company

Name	[redacted]
Address	[redacted]
Scope of business	EDC input support, Research procedures and contract procedures, Data management, Statistical analysis, etc.

12 Any other required information

No other required information need to be recorded.