HEADING OF THE INSTITUTION HOSTING THE STUDY
1/8 V.1 – 22 July 2025

INFORMATION SHEET AND INFORMED CONSENT FORM
FOR PATIENT PARTICIPATION IN A CLINICAL STUDY

Study Title:
International multicenter study on the Navitor/Navitor Vision transcatheter aortic valve (INTENSIVE Study)

Acronym: INTENSIVE

Protocol Version: V. 2.0 dated 18 July 2025

Study Sponsor: IRCCS Policlinico San Donato,
San Donato Milanese, Milan, Italy

Coordinating Study Investigator: Dr. Luca Testa

Registry in which the study has been or will be registered and identification code:
Identification code: _____
https://clinicaltrials.gov/

Study Site Name: IRCCS Policlinico San Donato

Principal Investigator: Dr. Luca Testa

Territorial Ethics Committee: CET Lombardia 1

Dear Patient,

This form explains why this study is being conducted and what your role will be should you decide to take part.

This informed consent form may contain terms that are difficult to understand. Please contact the study doctor or study staff if you require clarification of any terms or information that are unclear to you. It is important that you fully understand the content of this form.

Participation in the study is entirely voluntary. If you do not wish to participate, you are not required to do so. You will be guaranteed the best possible care regardless of your participation in the study. Refusal to participate will not involve any penalty or loss of benefits.

If you decide to participate in the study, you will be asked to sign, date, and print your name in the consent section of this form before any study-related activities may begin.

By signing this form, you declare that you:

- Have understood the contents of this document
- Consent to participate in the study

- Consent to the use of your personal and health data as described

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A. INFORMATION SECTION – GENERAL SUMMARY OF THE STUDY

This study aims to collect medical information and experiences related to the Navitor Transcatheter Aortic Valve Implantation (TAVI) System (Navitor valve, Navitor loading system, and FlexNav delivery system). The Navitor TAVI system is already approved for use in your country; therefore, this study is intended solely to collect additional information on the device's performance in real-world clinical practice.

DESCRIPTION OF THE NAVITOR TAVI SYSTEM

The Navitor valve is a replacement heart valve that is delivered via a catheter inserted through a puncture in the groin and advanced to the heart. The valve and its sealing skirt are made of bovine (cow) tissue and a fabric sewn onto a stent, or frame, which holds them in place. The stent portion of the valve is made of nitinol (a nickel-titanium alloy).

You may receive a version of the Navitor valve that includes three radiopaque markers, made of tantalum metal, sewn into the annular section of the valve to enhance valve visibility during deployment.

The Navitor valve is available in different sizes, and the physician will select the most appropriate size for your needs.

The Navitor valve has been approved for commercial use in your country for patients with severe aortic stenosis (narrowing of the aortic valve) who are at high or extreme risk for surgical aortic valve replacement.

The Navitor valve is loaded into a delivery system using the Navitor loading system, a two-part funnel system that compresses the stent to allow insertion into the delivery system. The FlexNav delivery system is part of the catheter and assists the study physician in positioning the valve in the heart. The delivery system is approximately the size of a ring finger.

The study physician will position the valve in the heart using echocardiography and fluoroscopy (angiographic imaging). After the valve is positioned, the delivery system will slowly expand the valve until it reaches its full size.

How many centers and patients will take part?

Approximately 1,000 patients will participate in the study across approximately 25 centers in Europe and the United Kingdom.

Is participation voluntary?

You may freely choose whether or not to participate in the study. Even after agreeing to participate, you may change your mind at any time.

What options do I have if I decide not to participate?

If you decide not to participate in the study, you will continue to be followed by the clinical center responsible for your care and will be treated using the best available therapeutic approaches.

What happens if I decide to participate?

If you decide to participate, you must first sign this informed consent form.

Your participation will last approximately 5½ years, for a total of nine visits, including the implant procedure. The implant procedure will be performed according to standard hospital clinical practice. This means the procedure would be the same regardless of your participation in the study.

The study includes the following nine visits:

- Baseline
- Implant
- Discharge
- 30-day follow-up
- 12-month follow-up
- Annual follow-up from Year 2 to Year 5

During the study, the following assessments are specifically related to the study and would not normally be performed as part of standard care:

- Stroke assessment scale (if applicable)
- Functional status questionnaire assessing daily activities and quality of life related to your heart condition
- Health status change assessment throughout the study duration

A complete schedule of visits and tests is provided in the next section, “What tests, assessments, and procedures are planned?”

What are the potential benefits?

You should not expect to receive any direct benefit from participating in this study. The information collected will contribute to a better understanding of treatment options for patients with aortic stenosis.

What are the possible risks?

The devices used in this study are approved and commercially available in your country. There are no new or additional risks resulting from participation. All devices and procedures will be used according to their approved indications and instructions for use.

Because this is a data collection study, the primary risk is loss of confidentiality. Other risks are the same as those associated with any TAVI procedure, regardless of study participation.

If you are pregnant or planning a pregnancy, discuss participation with the study physician. Patients who become pregnant during the study must contact the study physician immediately.

Is consent final? Can I withdraw?

You may withdraw from the study at any time and for any reason without providing justification.

If you withdraw, no additional data will be collected, but previously collected data will be retained to ensure correct analysis of study results.

Can participation be terminated without my consent?

Yes. The investigator may discontinue your participation without your consent if:

- You become pregnant (for female participants);
- The study is terminated by authorities or the sponsor.

B. INFORMATION SECTION – FURTHER DETAILS

1. What tests, assessments, and procedures are planned?

Baseline Visit
Includes eligibility assessment, medical history, physical exam, NYHA functional class, quality-of-life questionnaire (KCCQ), frailty index, echocardiography, blood tests, ECG, neurological assessment, and CT scan.

Implant Procedure
The Navitor valve will be implanted in a catheterization laboratory or operating room under sedation or general anesthesia. Access may be via the femoral artery or, if safer, via vessels near the shoulder.

If implantation of the Navitor valve is unsuccessful, an alternative commercially available transcatheter valve or surgical valve replacement may be performed. If no valve is implanted, you will be followed for 30 days and then withdrawn from the study.

Discharge Visit
Includes physical exam, medication review, ECG (if pacemaker implanted), echocardiography, blood tests, neurological assessment, and health status evaluation.

Follow-Up Visits
Scheduled at 30 days, 12 months, and annually from Year 2 to Year 5. Visits last approximately 1.5 hours and may be conducted by phone if necessary.

Unscheduled Visits
Additional imaging, neurological assessments after stroke, and health status evaluations may be included.

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2. Should my general practitioner be informed?

Yes. It is important that your primary care physician is informed of your participation.

3. Will participation involve costs or compensation?

There are no costs to you. No compensation or reimbursement is provided.

4. What happens if I am harmed?

Due to the observational nature of the study, no specific insurance is provided; however, the hospital has general insurance coverage. You will receive appropriate medical treatment if injury or complications occur.

5. How can I access study results?

After study completion, results will be analyzed and shared with the scientific community. Participants may request general study results from the investigator.

6. Has the study been approved by an Ethics Committee?

Yes. The study protocol was approved by CET Lombardia 1 and complies with Good Clinical Practice and the Declaration of Helsinki.

7. Who can I contact for further information?

For questions about the study, contact:
Dr. _____
Email: _____
Phone: _____

CONSENT AND AUTHORIZATION TO PARTICIPATE IN THIS CLINICAL STUDY

By signing this form, you acknowledge that you have read the information contained in this document and that you have decided to participate in the study. You will be provided with a signed copy of this form for your records.

- I have read all the information provided above in this consent and authorization form.
- I have had the opportunity to ask questions and have received satisfactory answers regarding any points that were unclear.
- I voluntarily agree to participate in this study and to comply with the related procedures.
- I confirm that my coded data collected during the study will be used for analysis and that, once stripped of identifying elements or anonymized, they may be included in publications.
- I understand that I am free to refuse to participate in the proposed study without providing any explanation and without affecting my medical care or my legal rights.
- I understand that I am free to withdraw from the proposed study at any time, without providing any explanation and without affecting my medical care or my legal rights.
- I consent to the research partners, the Ethics Committee, and regulatory authorities accessing and using my medical data and personal information in accordance with what is described in this form.
- I authorize the study staff to inform my treating physician of my participation in this study.
- I authorize the study physician to contact the population registry office of the last known municipality of residence, should I be unreachable for follow-up visits, in order to obtain information regarding my whereabouts and health status.
- I authorize the study physician to contact my treating physician, should I be unreachable for follow-up visits, in order to obtain information regarding my whereabouts and health status.

Participant's full name (printed): _____

Signature: _____ Date: _____ Time: _____

Full name of the physician obtaining consent (printed): _____

Signature: _____ Date: _____