PEERLESS study

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The primary study objective is to compare the clinical outcomes of patients treated with the FlowTriever System versus Catheter-Directed Thrombolysis (CDT) for use in the treatment of acute intermediate-high-risk pulmonary embolism (PE).

Ethical review	Approved WMO
Status	Will not start
Health condition type	Vascular therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON51587

Source
ToetsingOnline

Brief title
PEERLESS study

Condition

- Vascular therapeutic procedures
- Embolism and thrombosis

Synonym
Pulmonary embolism

Research involving
Human

Sponsors and support

Primary sponsor: Inari Medical Europe GmbH
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: Catheter-directed, FlowTriever system, Pulmonary embolism, Thromboloysis

Outcome measures

Primary outcome

The primary endpoint is a composite clinical endpoint constructed as a win ratio, a hierarchy of the following, assessed at hospital discharge or at 7 days after the index procedure, whichever is sooner:

1. All-cause mortality, or
2. Intracranial hemorrhage (ICH), or
3. Major bleeding per ISTH definition4, or
4. Clinical deterioration defined by hemodynamic or respiratory worsening, and/or escalation to a bailout therapy, or
5. ICU admission and ICU length-of-stay during the index hospitalization and following the index procedure.

Secondary outcome

The secondary endpoints of the study will assess safety, effectiveness, and utility measures, as follows:

* Composite clinical endpoint constructed as a win ratio hierarchy of the following four components, assessed at hospital discharge or at 7 days after the index procedure, whichever is sooner:
o All-cause mortality, or
o Intracranial hemorrhage (ICH), or
o Major bleeding per ISTH definition4, or

o Clinical deterioration defined by hemodynamic or respiratory worsening, and/or escalation to a bailout therapy

* Individual components of the win ratio composite endpoint, assessed at hospital discharge or at 7 days after the index procedure, whichever is sooner:
o All-cause mortality
o Intracranial hemorrhage (ICH)
o Major bleeding per ISTH4 definition
o Clinical deterioration defined by hemodynamic or respiratory worsening, and/or escalation to a bailout therapy
o ICU admission and ICU length of stay during the index hospitalization and following the index procedure

* All-cause mortality within 30 days from index procedure
* PE-related and all-cause readmission within 30 days from index procedure
* Device and drug-related serious adverse events through the 30 day visit
* Clinically Relevant Non-Major (CRNM) and Minor bleeding events through hospital discharge or at 7 days after the index procedure, whichever is sooner
* Change in right-ventricular/left-ventricular (RV/LV) ratio from baseline to 24 hour visit, as measured by echocardiography or CT
* mMRC Dyspnea score at 24 hour visit and 30 day visit
* Length of total hospital stay and post-index-procedure hospital stay (to a maximum of 30 days)
* Disease-specific and general health-related quality of life at the 30 day

visit (PEmb-QoL and EQ-5D-5L)

Study description

Background summary

Pulmonary embolism (PE) is a debilitating and potentially lethal disease, leading to an estimated 300,000 hospitalizations per year in the US, and over 400,000 PE events in Europe in 2004 with 10-30% mortality. PE and deep vein thrombosis (DVT) are the 2 main clinical consequences of venous thromboembolism (VTE), which together lead to over 500,000 annual hospitalizations in the US, and a similar number in Europe. While a reduction in mortality was seen over that time period, mortality in 2012 still ranged from 1.6% to 39.1%, depending on the severity of the disease. While small PEs may remain asymptomatic and go unnoticed, larger emboli can result in significant pulmonary artery obstruction, leading to right heart decompensation and mortality. The goal of a successful interventional procedure is to restore RV outflow through the pulmonary artery, thereby disrupting the potentially lethal cascade towards hemodynamic collapse. However, there remains a strong clinical need to develop a reliable, rapid, percutaneous method of thrombus removal for the treatment of clinically significant acute PE. The need is especially strong for a mechanical method that does not rely on the use of thrombolytics, as physicians are reluctant to administer thrombolytics given the high bleeding risk and because many patients cannot tolerate lytics. The FlowTriever System was developed to meet this need to rapidly restore blood flow through the pulmonary vasculature in patients experiencing acute submassive or massive pulmonary embolism. However, clinical data from prospective, randomized control trials are still lacking for FlowTriever and other advanced therapies.

Study objective

The primary study objective is to compare the clinical outcomes of patients treated with the FlowTriever System versus Catheter-Directed Thrombolysis (CDT) for use in the treatment of acute intermediate-high-risk pulmonary embolism (PE).

Study design

This study is a prospective, multicenter, randomized controlled trial of the FlowTriever System compared to CDT for acute intermediate-high-risk PE, and includes a non-randomized cohort for subjects with an absolute contraindication to thrombolytics. The study will collect data on demographics, comorbidities, details from the PE diagnosis and treatment, and clinical outcomes through 30-day follow up.

Randomized Controlled Trial Cohort (RCT Cohort):

This study is a prospective, multicenter, randomized controlled trial of the FlowTriever System compared to Catheter-Directed Thrombolysis (CDT) for treatment of acute intermediate-high-risk PE.

Non-Randomized Absolute Contraindication to Thrombolytics Cohort (Contraindication Cohort):

Subjects who meet study eligibility criteria and who have an absolute contraindication to thrombolytics, whose initial planned primary treatment strategy includes FlowTriever, will be evaluated as part of the Contraindication Cohort. The same RCT Cohort clinical assessments and follow up schedule will be administered in this Contraindication Cohort.

Intervention

N/A

Study burden and risks

There is an optional invasive additional measurement for Catheter-directed thrombolysis patients. Once the procedure is finished the catheters are typically removed right away. Optionally and if really required, the post PA pressure measurements can be collected but reopening of the access area would be required (6 hours post procedure).

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Subjects must meet each of the following criteria to be included in the study:
1. Age * 18 years
2. Echo, computed tomographic pulmonary angiography (CTPA), or pulmonary angiographic evidence of any proximal filling defect in at least one main or lobar pulmonary artery
3. Classification of intermediate-high-risk PE by ESC Guidelines 20191, including ALL of the following:
a. Clinical signs and symptoms consistent with acute PE, or PESI class III-V, or sPESI *1
AND
b. Hemodynamically stable
AND
c. RV dysfunction on echocardiography or CT
AND
d. Elevated cardiac troponin levels
4. Intervention planned to begin within 72 hours of the later of either
a. Confirmed PE diagnosis
OR
b. If transferring from another hospital, arrival at the treating hospital
5. Symptom onset within 14 days of confirmed PE diagnosis

Exclusion criteria

Subjects will be excluded from the study for any of the following criteria:
1. Unable to anticoagulate with heparin, enoxaparin or other parenteral antithrombin
2. Index presentation with hemodynamic instability that are part of the high-

risk PE definition in the ESC Guidelines 20191, including ANY of the following:
a. Cardiac arrest OR
b. Systolic BP < 90 mmHg or vasopressors required to achieve a BP *90 mmHg despite adequate filling status, AND end-organ hypoperfusion
OR
c. Systolic BP < 90 mmHg or systolic BP drop *40 mmHg, lasting longer than 15 min and not caused by new-onset arrhythmia, hypovolemia, or sepsis
3. Known sensitivity to radiographic contrast agents that, in the Investigator*s opinion, cannot be adequately pre-treated
4. Imaging evidence or other evidence that suggests, in the opinion of the Investigator, the patient is not appropriate for catheter-based intervention (e.g. inability to navigate to target location, clot limited to segmental/subsegmental distribution, predominately chronic clot)
5. Patient has right heart clot in transit identified at baseline screening
6. Life expectancy < 30 days (e.g stage 4 cancer or severe COVID-19 infection), as determined by the Investigator
7. Current participation in another drug or device study that, in the Investigator*s opinion, would interfere with participation in this study
8. Current or history of chronic thromboembolic pulmonary hypertension (CTEPH) or chronic thromboembolic disease (CTED) diagnosis, per ESC 2019 guidelines1
9. Invasive systolic PA pressure *70 mmHg prior to study device entering the body
10. Administration of bolus or drip/infusion thrombolytic therapy or mechanical thrombectomy for the index PE event within 48 hours prior to enrollment
11. Ventriculararrhythmiasrefractorytotreatmentatthetimeofenrollment
12. Knowntohaveheparin-inducedthrombocytopenia(HIT)
13. Subject has any condition for which, in the opinion of the Investigator, participation would not be in the best interest of the subject (e.g., compromise the well-being or that could prevent, limit, or confound the protocol-specified assessments)
14. Subject has previously completed or withdrawn from this study
15. Patient unwilling or unable to conduct the follow up visits per protocol.

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active

Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	12
Type:	Anticipated

Medical products/devices used

Generic name:	FlowTriever System
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	12-10-2022
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	08-12-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-05-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL81035.078.22