A multicenter, randomized, open-label, blinded endpoint evaluation, phase 3 study comparing the effect of abelacimab relative to dalteparin on venous thromboembolism (VTE) recurrence and bleeding in patients with gastrointestinal (GI)/genitourinary (GU) cancer associated VTE

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This study has been transitioned to CTIS with ID 2024-513992-42-00 check the CTIS register for the current data. The primary objective of this study is to assess whether abelacimab is non-inferior to dalteparin for preventing VTE recurrence through…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Embolism and thrombosis
Study type	Interventional

Summary

ID

NL-OMON53552

Source
ToetsingOnline

Brief title
MAGNOLIA

Condition

- Embolism and thrombosis

Synonym
venous thromboembolism

Research involving
Human

Sponsors and support

Primary sponsor: Anthos Therapeutics, Inc.
Source(s) of monetary or material Support: Anthos Therapeutics;Inc.

Intervention

Keyword: bleeding, cancer associated VTE, venous thromboembolism (VTE) recurrence

Outcome measures

Primary outcome

The primary objective of this study is to assess whether abelacimab is

non-inferior to dalteparin for preventing VTE recurrence through 6 months

post randomization in patients with GI or GU cancer and recently diagnosed VTE.

If non-inferiority is demonstrated, then superiority will be

assessed.

Secondary outcome

o To assess whether abelacimab is superior to dalteparin for preventing

occurrence of the composite of major or CRNM bleeding through 6

months post-randomization

o To assess whether abelacimab is superior to dalteparin on net clinical

benefit defined as survival without VTE recurrence, or major or CRNM

bleeding events through 6 months post-randomization

o To assess whether abelacimab is superior to dalteparin on the rate of

permanent treatment discontinuation not due to death through 6

months post-randomization

o To assess whether abelacimab is superior to dalteparin for preventing

occurrence of CRNM bleeding events through 6 months post

randomization

o To assess whether abelacimab is superior to dalteparin for preventing

occurrence of major bleeding events through 6 months postrandomization

o To assess whether abelacimab is superior to dalteparin for preventing

occurrence of the composite of GI major and CRNM bleeding through

6 months post-randomization

o To evaluate safety and tolerability of abelacimab relative to dalteparin

through 6 months post randomization and to assess the incidence rate

of injection site reactions, hypersensitivity reactions and immunogenicity in

patients treated with abelacimab

Study description

Background summary

The goal of developing a new treatment for CAT, and especially patients with CAT who are at high risk for bleeding, is to maintain the same level of efficacy as current agents but with less bleeding and greater tolerability.

The purpose of this phase 3 study is to assess whether monthly treatment with abelacimab is non-inferior to daily administration of dalteparin in preventing VTE recurrence but is superior in the rate of bleeding in patients with GI/GU cancer and recently diagnosed VTE. This study
will support worldwide registration of abelacimab for the treatment of CA VTE.

Study objective

This study has been transitioned to CTIS with ID 2024-513992-42-00 check the CTIS register for the current data.

The primary objective of this study is to assess whether abelacimab is non-inferior to dalteparin for preventing VTE recurrence through 6 months post randomization in patients with GI or GU cancer and recently diagnosed VTE. If non-inferiority is demonstrated, then superiority will be assessed.

Study design

This is a randomized, open-label, blinded endpoint evaluation (PROBE), active-controlled, study.

Intervention

• Abelacimab 150 mg iv on Day 1 then, starting approximately 30 days later, abelacimab 150 mg sc every month for an additional 5 months (sc administration planned on Days 31, 61, 91, 121, and 151 ±5 days).

• Dalteparin 200 IU/kg/day sc from Day 1 to Day 30 then dalteparin 150 IU/kg/day sc from Day 31 to Day 181. (The maximal daily dose should not exceed 18,000 IU).

Study burden and risks

Side effects from study medication abelacimab and dalteparin.

• Injection site reaction - If you receive injections with abelacimab, you may have pain, swelling, bruising, bleeding, or redness at the injection site.
• Blood samples - Risks associated with blood collection include pain, swelling and/or bruising at the insertion site of the needle. Although rare, localized clot formation, infections and nerve damage may occur. Light-headedness and/or fainting may also occur during or shortly after the blood draw.
• ECG - You may have mild irritation, slight redness, or itching at the sites on your skin where the recording patches are placed. If male, it may be necessary to shave the area on your chest for placement of ECG tabs directly on skin.

Abelacimab may help to effectively treat the clot in the body and help prevent blood clots from forming again. However, there is noguarantee that there will be any benefit to the subject.

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

• Male or female subjects >=18 years old or other legal maturity age according to the country of residence
• Confirmed GI (colorectal, pancreatic, gastric, esophageal, gastro-esophageal junction or hepatobiliary) or confirmed GU (renal, ureteral, bladder, prostate, or urethra) cancers if:
o Unresectable, locally advanced, metastatic, or non-metastatic GI/GU cancer and
o No intended curative surgery during the study
• Confirmed symptomatic or incidental proximal lower limb acute DVT (i.e., popliteal, femoral, iliac, and/or inferior vena cava vein thrombosis) and/or a confirmed symptomatic PE, or an incidental PE in a segmental, or larger pulmonary artery. Patients are eligible within 72 hours from diagnosis of the qualifying VTE.
• Anticoagulation therapy with LMWH for at least 6 months is indicated.
• Able to provide written informed consent

Exclusion criteria

• Thrombectomy, insertion of a caval filter or use of a fibrinolytic agent to treat the current (index) DVT and/or PE
• More than 72 hours of pre-treatment with therapeutic doses of UFH, LMWH, or other anticoagulants
• An indication to continue treatment with therapeutic doses of an anticoagulant other than that for VTE treatment prior to randomization (e.g., AF, mechanical heart valve, prior VTE)
• PE leading to hemodynamic instability (blood pressure [BP] <90 mmHg or shock)
• Acute ischemic or hemorrhagic stroke or intracranial hemorrhage within 4 weeks of screening
• Brain trauma or a cerebral or spinal cord surgery within 4 weeks of screening
• Need for aspirin in a dosage of >100 mg/day or any other antiplatelet agent alone or in combination with aspirin
• Bleeding requiring medical attention at the time of randomization or within the preceding 4 weeks
• Planned major surgery at baseline
• History of heparin-induced thrombocytopenia
• Primary brain cancer or untreated intracranial metastasis
• Eastern Cooperative Oncology Group (ECOG) performance status of 3 or 4 at screening
• Life expectancy <3 months at randomization
• Calculated creatinine clearance (CrCl) <30 mL/min (Cockcroft-Gault equation)
• Platelet count <50,000/mm3
• Hemoglobin <8 g/dL
• Acute hepatitis, chronic active hepatitis, liver cirrhosis; or an alanine aminotransferase (ALT) >=3 x and/or bilirubin >=2 x upper limit of normal (ULN) in absence of clinical explanation
• Uncontrolled hypertension (systolic BP >180 mm Hg or diastolic BP >100 mm Hg) despite antihypertensive treatment
• Women of child-bearing potential (WOCBP) who are unwilling or unable to use highly effective contraceptive measures during the study from screening up to 3 days after last treatment of dalteparin or 100 days after administration of abelacimab (See Section 5.3.6 for highly effective contraceptive measures)
• Sexually active males with sexual partners of childbearing potential must agree to use a condom or other reliable contraceptive measure up to 3 days after last treatment of dalteparin or 100 days after administration of abelacimab.
• Pregnant or breast-feeding women
• History of hypersensitivity to any of the study drugs (including dalteparin) or its excipients, to drugs of similar chemical classes, or any contraindication listed in the label for dalteparin
• Subjects with any condition that in the Investigator*s judgement would place

the subject at increased risk of harm if he/she participated in the study
• Use of other investigational (not-registered) drugs within 5 half-lives prior to enrollment or until the expected PD effect has returned to baseline, whichever is longer. Participation in academic non-interventional studies or interventional studies testing different strategies or different combinations of registered drugs is permitted.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-04-2023
Enrollment:	50
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Abelacimab
Generic name:	Abelacimab
Product type:	Medicine
Brand name:	Fragmin
Generic name:	Dalteparin
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	05-04-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	25-10-2022
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	02-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	18-11-2022
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	03-02-2023
Application type:	Amendment
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Approved WMO Date:	07-02-2023
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Approved WMO Date:	24-11-2023
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
EU-CTR	CTIS2024-513992-42-00
EudraCT	EUCTR2021-003085-12-NL
ClinicalTrials.gov	NCT05171075
CCMO	NL80501.018.22