Pilot Study for assessing Diagnostic Techniques for Central Venous Catheter-related Venous Thromboembolism

Published: 02-11-2010
Last updated: 06-05-2024

Primary Objectives:To (1) Assess the feasibility and tolerability of performing US and/or contrast-enhanced MRI in children with central venous catheters (CVCs) or peripherally inserted central catheters (PICC lines); (2) assess the accuracy of US...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Embolism and thrombosis
Study type	Observational invasive

Summary

ID

NL-OMON38386

Source
ToetsingOnline

Brief title
CV185-077

Condition

- Embolism and thrombosis

Synonym
Venous Thromboembolism; Vein blockage due to clot formation

Research involving
Human

Sponsors and support

Primary sponsor: Bristol-Myers Squibb
Source(s) of monetary or material Support: Pharmaceutical company

Intervention

Keyword: Central Venous Catheter, Paediatric, Pilot, Venous Thromboembolism

Outcome measures

Primary outcome

The primary outcome measures will include:

* The number of subjects recruited into the study that are able to undergo each one of the imaging procedures (ultrasound and MRI) that are performed at Visit 1. Visit 1, is defined for Cohort A subjects as day 40 ± 20 days from the placement of the CVC, or if possible within 72 hours after a CVC is removed or lost. For Cohort B subjects Visit 1 is defined as within 7 days of initiation of symptoms of a CVC-related DVT or within 7 days of an incidental diagnosis of CVC-related DVT by radiographic imaging.

* The frequency and nature of difficulties encountered during each one of the imaging procedures that are performed at Visit 1. Visit 1, is defined for Cohort A subjects as day 40 ± 20 days from the placement of the CVC, or if possible within 72 hours after a CVC is removed or lost. For Cohort B subjects Visit 1 is defined as within 7 days of initiation of symptoms of a CVC-related DVT or within 7 days of an incidental diagnosis of CVC-related DVT by radiographic imaging.

* Frequency of subjects with a DVT detected by the ultrasound and/or MRI at Visit 1 and confirmed by adjudication. Visit 1, is defined for Cohort A subjects as day 40 ± 20 days from the placement of the CVC, or if possible within 72 hours after a CVC is removed or lost. For Cohort B subjects Visit 1 is defined as within 7 days of initiation of symptoms of a CVC-related DVT or

within 7 days of an incidental diagnosis of CVC-related DVT by radiographic imaging.

Secondary outcome

The secondary outcomes measures will include:

* Frequency of subjects in Cohort A with asymptomatic for CVC-related DVT identified by the investigator at enrollment and confirmed by at least one adjudicated diagnostic imaging procedure performed at Visit 1. Visit 1, is defined for Cohort A subjects as day 40 ± 20 days from the placement of the CVC, or if possible within 72 hours after a CVC is removed or lost.

* Frequency of symptomatic subjects in Cohort B with CVC-related DVT identified by the investigator at enrollment and confirmed by at least one adjudicated diagnostic imaging procedure performed at Visit 1. Visit 1, is defined for defined for Cohort B subjects as within 7 days of initiation of symptoms of a CVC-related DVT or within 7 days of an incidental diagnosis of CVC-related DVT by radiographic imaging.

* Frequency of subjects in Cohort B with or without symptoms for CVC-related DVT, who have been incidentally identified by radiographic imaging performed for other clinical reasons as having a CVC-related DVT in the veins where the current catheter is placed, identified by the investigator at enrollment and confirmed by at least one adjudicated diagnostic imaging procedure performed at Visit 1. Visit 1 is defined for Cohort B subjects as within 7 days of initiation of symptoms of a CVC-related DVT or within 7 days of an incidental

diagnosis of CVC-related DVT by radiographic imaging.

* Frequency of asymptomatic subjects enrolled in Cohort A developing symptoms of a VTE, including DVT or PE, identified by the investigator between enrollment and Visit 1 and confirmed by at least one adjudicated diagnostic imaging procedure performed within 7 days of the initiation of symptoms. The period between enrollment and Visit 1 is defined for Cohort A subjects as from the time of enrollment up to 60 days after the CVC has been placed, or from the time of enrollment up to 72 hours after the CVC is removed or lost

*Frequency of adjudicated PE events (symptomatic or asymptomatic) identified during the course of the study as defined from enrollment up to 30 days following the study radiographic procedures (MRI and/or Ultrasound).
* Frequency of adjudicated death events occurred during the course of the study as defined from enrollment up to 30 days following the study radiographic procedures (MRI and/or Ultrasound).

Study description

Background summary

Deep Vein thrombosis (DVT) occurs in children as a secondary complication of multiple risk factors related to underlying disease and its treatment. DVT is most commonly related to the presence of central venous catheters (CVC), particularly in patients with cancer.

Children with a CVC develop DVT in 25 - 70% of cases depending on age and the underlying disease. Reported incidence rates also depend on the imaging procedure used for diagnosis and trial design. About two thirds of DVT in

children occur in the upper body central venous system, reflecting the most common location of the CVC placement. Most CVC-related DVT are asymptomatic, however, there is a growing body of information that asymptomatic DVTs are of clinical significance.

Ultrasound (US) is the most frequently used test for diagnosis of DVT because of its ease of use, non-invasiveness, and its excellent accuracy for diagnosis of DVT in the lower extremities. For diagnosis of CVC-related DVT in the upper venous system, a combination of venography and ultrasound is currently considered the reference standard. However, conventional venography has limitations, particularly in children, because of its invasive nature, technical demands, costs, adverse effects associated with nephrotoxic contrast media, and radiation exposure.

Contrast-enhanced magnetic resonance imaging (MRI) is an attractive alternative allowing comprehensive imaging of the central venous system. Advantages of contrast-enhanced MRI are that it is minimally invasive, does not involve radiation, and magnetic resonance contrast media are well tolerated. An added value of contrast-enhanced magnetic resonance is that it allows simultaneous evaluation of the pulmonary vasculature for presence of Pulmonary Embolism (PE).

To date, only two pediatric studies have reported on the use of contrast-enhanced MRI in children in the lower and upper venous system, but there was no systematic comparison to other diagnostic imaging procedures. The feasibility and diagnostic accuracy of contrast enhanced MRI for CVC-related DVT in children remains to be established.

Study objective

Primary Objectives:
To (1) Assess the feasibility and tolerability of performing US and/or contrast-enhanced MRI in children with central venous catheters (CVCs) or peripherally inserted central catheters (PICC lines); (2) assess the accuracy of US and/or MRI for detection of CVC-related DVT in the venous region of CVC placement (jugular, subclavian, and femoral CVC) and identify the best combination of tests for reliable assessment of CVC-related DVT.
Secondary Objectives:
To (1) assess the accuracy of clinical diagnosis of DVT versus US, MRI, or both; (2) Assess the event rate of adjudicated PE; (3) Assess the event rate of adjuducated death.

Study design

CV185077 is an interventional non-therapeutic study to select the diagnostic techniques to detect DVT in children (full-term newborn to < 18 years old) with

an indwelling CVC. The children will be subdivided into three cohorts.

Cohort A (asymptomatic subjects) will have a CVC placed for at least 40 ± 20 for which Day 0 is the day of catheter placement and Day 40 ± 20 is the day of the diagnostic imaging procedure. Asymptomatic subjects will have their diagnostic imaging procedures done without sedation or anesthesia. Subjects enrolled in Cohort A who develop symptoms of a DVT prior to their diagnostic imaging procedures will be switched into Cohort B.

Cohort B (symptomatic subjects) will consist of those subjects who have an indwelling CVC and have symptoms of a suspected DVT or subjects who have been incidentally-identified by radiographic imaging (imaging modalities to diagnose an incidental CVC-related DVT may include, but is not exclusive of Echocardiogram, CT scan, MRI, or Ultrasound) performed for other clinical reasons, as having a CVC-related DVT in the veins where the current catheter is placed and may not have symptoms of a DVT. Diagnostic imaging procedures should be initiated within 7 days of symptoms of a CVC-related DVT or within 7 days of the incidental diagnosis of a CVC-related DVT by radiographic imaging. Symptomatic subjects may undergo sedation/anesthesia for the diagnostic imaging procedures if approved by the subject care team, parents, and subject (when older than 12 years). All Cohort B subjects are allowed to be started on therapeutic anti-coagulation for the treatment of their thrombosis, if the investigator considers appropriate. If anticoagulation is started, the second radiographic procedure should be performed within 24-hours of the first radiographic procedure.

Cohort C (asymptomatic subjects) will collect diagnostic imaging procedures for subjects up to 18 years of age who have a CVC in place and who are scheduled to undergo a contrast enhanced MRI in any part of their body as part of their clinical care and will allow the diagnostic imaging procedure to include the area around the CVC.

The final visit will occur within 30 days after the US/contrast-enhanced MRI to assess for any non-serious and serious adverse events.

An independent Central Adjudication Committee (ICAC) will adjudicate all ultrasounds and contrast-enhanced MRIs for suspected symptomatic and asymptomatic VTEs.

Intervention

Performance of contrast-enhanced MR Imaging with Gadolinium contrast injection.

Administration of the anesthesia or sedation as per standard of care for symptomatic patients.

Study burden and risks

This study is evaluating sophisticated diagnostic imaging procedures for CVC-DVT detection that will allow for proper diagnostic techniques to be used in safety and efficacy studies for a new anti-coagulant, apixaban, for prevention of catheter related thrombosis in children.

Asymptomatic children in cohort A will undergo ultrasonography and MRI after 20-60 days with a catheter. Ultrasonography is an easy to perform, painless, non-invasive method without radiation. For MRI the children need to receive contrast. Problems with contrast are very rare and occur mainly in patients with moderate-severe kidney failure. These patients are not eligible for this study. The contrast will be given using the CVC, so without venapuncture. Only gadolinium products approved by the regulatory authorities and ethics committees for children in each age category will be used.

Patients in cohort C will get MRI for other reasons and according to this study an additional ultrasonography. Ultrasonography is a non-invasive method without radiation, as described above.
For children in cohort A and C asymptomatic DVT might be diagnosed. The physician could decide to treat these patients with anticoagulation in case of severe thrombosis and pulmonary embolism to prevent enlargement of thrombi or to do a follow-up diagnostic test to follow the thrombus.

In symptomatic children (cohort B) ultrasonography is used to detect DVT, usually in combination with venography. In this study a MRI will be used instead of venography. In contrast to venography, MRI is not invasive (contrast can be injected in the central venous catheter instead of the veins of the hand), and does not involve radiation. Furthermore, it allows simultaneous evaluation of the pulmonary vasculature for presence of pulmonary embolism which is not possible with venography.

Contacts

Public
Bristol-Myers Squibb

Vijzelmolenlaan 9
3440 AM Woerden
NL
Scientific
Bristol-Myers Squibb

Vijzelmolenlaan 9

3440 AM Woerden
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Children (2-11 years)

Inclusion criteria

Signed Written Informed Consent
Target Population
2) Functioning CVC in the upper or lower venous system (eg, jugular, subclavian; femoral vein)
3) Cohort A: Asymptomatic subjects having placement of a new, indwelling CVC in the last 40±20 days
4) Cohort B: Subjects who have experienced symptoms for a CVC-related DVT with a CVC in place or subjects who have been incidentally identified by radiographic imaging (imaging modalities to diagnose an incidental CVC-related DVT may include, but is not exclusive of Echocardiogram, CT scan, MRI, or Ultrasound) performed for other clinical reasons, as having a CVC-related DVT in the veins where the current catheter is placed.;Age and Reproductive Status
5) Males and females from full-term newborns to < 18 years
6) Women must have a negative serum or urine pregnancy test

Exclusion criteria

1) Failure to provide written consent from parents or guardians
Target Disease Exceptions
2) For cohort A subjects only, present therapeutic dosing of systemic anticoagulant, systemic thromboprophylaxis, or antiplatelet therapy. Local thromboprophylaxis [flushes, low dose infusions of heparin of up to 5 u/kg/hr or locks with heparin, urokinase, t-plasminogen activator] according to standard-of-care at the respective

center will be allowed.;Medical History and Concurrent Diseases
3) Children unable to undergo contrast-enhanced MRI
4) Pacemaker, osteosynthesis material implanted within the last month;Physical and Laboratory Test Findings
5) Abnormal baseline laboratory test results:
* Renal function < 50% of normal for age and size
6) Positive pregnancy test;Allergies and Adverse Drug Reaction
7) Allergy to gadolinium;Other Exclusion Criteria
8) Prisoners or subjects who are involuntarily incarcerated
9) Subjects who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness.

Study design

Design

Study phase:	2
Study type:	Observational invasive
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	03-03-2011
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Application type:	First submission
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
ClinicalTrials.gov	NCT01137578
CCMO	NL32819.018.10