A Phase 3, Randomized, Single-Blind, Controlled Trial of Topical Fibrocaps* in Intraoperative Surgical Haemostasis

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Primary:The primary objective of the study is to demonstrate the superiority of Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, for achieving hemostasis in subjects undergoing spine, liver, vascular or soft tissue surgery, when...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatic and hepatobiliary disorders
Study type	Interventional

Summary

ID

NL-OMON39278

Source
ToetsingOnline

Brief title
FINISH-3

Condition

- Hepatic and hepatobiliary disorders
- Soft tissue therapeutic procedures
- Vascular disorders NEC

Synonym
Liver resection, Liver surgery, soft tissue surgery, spinal surgery, vasculair surgery

Research involving
Human

Sponsors and support

Primary sponsor: ProFibrix

Source(s) of monetary or material Support: ProFibrix

Intervention

Keyword: Fibrin, hemostasis, sealant, surgical

Outcome measures

Primary outcome

Primary:

Efficacy: Time to hemostasis (TTH) within the 5-minute TTH assessment period by treatment group within each surgical indication.

Secondary outcome

Efficacy: TTH-related endpoints include: restricted mean TTH, and proportion of subjects achieving hemostasis within 3 and 5 minutes by treatment group within each surgical indication. Additional endpoints include the use of alternative hemostatic agents at the TBS, transfusion requirements (RBC usage through Day 29) and re-operation at the TBS for bleeding complications by treatment group within each surgical indication.

Study description

Background summary

The intended benefit of Fibrocaps application is to support local hemostasis, especially in the situations where hemostatic measures based in conventional surgical techniques as suture, ligature or cautery may be ineffective or impractical.

Study objective

Primary:
The primary objective of the study is to demonstrate the superiority of Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, for

achieving hemostasis in subjects undergoing spine, liver, vascular or soft tissue surgery, when control of mild to moderate bleeding by standard surgical techniques is ineffective and/or impractical

Secondary:
Secondary study objectives are to further characterize the efficacy and safety profiles of Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, in subjects undergoing spine, liver, vascular or soft tissue surgery, when control of mild to moderate bleeding by standard surgical techniques is ineffective and/or impractical.

Study design

Study Design:
This is a Phase 3, international, multi-center, randomized, single-blind, controlled trial in subjects undergoing spinal surgery, hepatic resection, vascular surgery and soft tissue dissection surgery.
Subjects will provide written informed consent prior to undergoing any protocol related assessments or procedures, which may occur up to 30 days prior to surgery. After establishing eligibility during screening and confirming continued eligibility on the day of surgery (Day 1), subjects will be randomized in a single-blinded manner, in a 2:1 ratio to treatment with Fibrocaps in combination with an absorbable gelatin sponge (active group; F+G) or gelatin sponge alone (control group; G) when an appropriate TBS is identified. Subjects who are randomized but not treated with study drug will be withdrawn from the study and may be replaced. Reasons for not receiving study drug include but are not limited to lack of an
appropriate TTH evaluation site, severe bleeding or a change in surgical procedure after the subject has been randomized.
During a surgical procedure on Day 1 (Visit 2), subjects will be initially treated with up to one vial of Fibrocaps (1 g) plus gelatin sponge or gelatin sponge alone at the TBS and the TTH assessed every 30 seconds for up to 5 minutes. Bleeding appropriate for TTH evaluation is defined as mild to moderate bleeding, either on its own or remaining after brisk/severe bleeding has been controlled by standard surgical modalities. Subjects may be retreated with their assigned treatment as necessary during the 5-minute TTH assessment period, with up to a maximum of 3 vials of Fibrocaps (3 g) in total. Subjects who do not achieve hemostasis within 5 minutes will be considered treatment failures and treated with an alternative topical hemostatic agent or device of the surgeons choosing provided it does not contain thrombin for the subject*s randomized to Fibrocaps since it may impact the interpretation of the immunogenicity results at the end of the study. Subjects assigned to the control arm of *gelatin sponge alone* may be treated with thrombin-containing alternative hemostats after the TTH assessment period has elapsed at the discretion of the Investigator.

The alternative hemostat used should be recorded in the eCRF. Subjects who

achieve hemostasis within 5 minutes, but experience a re-bleeding before the 5 minute TTH assessment period has ended, will be considered hemostatic failures and may be treated with the assigned treatment or an alternative topical hemostatic agent or device of the surgeons choosing provided it does not contain thrombin.

At any time after hemostasis has been achieved at the TBS, the remaining assigned treatment may be used at additional appropriate bleeding sites that are part of the primary surgical procedure. However, all of the remaining Fibrocaps should not be used until after the 5-minute assessment period has elapsed in order to ensure that adequate Fibrocaps is available to use in the event of re-bleeding from the TBS.

The amount of study drug applied and the incidence of hemostasis achieved at these additional sites are recorded. The primary efficacy analysis will not include hemostasis data from these additional bleeding sites. Subjects will undergo a safety evaluation consisting of a targeted physical exam and clinical labs on Day 2 (Visit 3), which may be conducted on Day 1 and over the phone if the subject surgical procedure was performed as an outpatient, and a final safety follow-up evaluation visit on Day 29 (Visit 4, End of Study).

Intervention

The operation will be performed according to local standard surgical procedures. Patients will be randomized to either the active or in the control group (2:1). Patients in the active group will be treated with Fibrocaps (applied with or without Fibrospray) in combination with a gelatin sponge. Patients in the control group will be treated with only the gelatin sponge.
The Fibrospray is used for liver and soft tissue surgery and is optional for vasculaire and spinal surgery. The fibrospray works with compressed air from a central compressed air supply at the OK or via a compressed air tank. The fibrospray is connected via a pressure regulator and a filter. The Fibrocaps ampoule is connected to the fibrospray and sprayed with a distance of 5cm in the wound area.
In spinal and vascular surgery with a smaller wound area fibrocaps may applied as a thin layer directly from the ampoule in the wound area, and after the wound is covered with a gelatin sponge (spongostan) gently pressed with a sterile gauze.
Fibrocaps may also be applied to the gelatin sponge, then applied onto the wound area, followed by manual pressure applied with a sterile gauze.

To see if hemostasis is achieved, from the moment of the start of the therapy every 30 seconds, the loss of blood through and around the gelatin sponge will be observed until hemostasis has been reached, or the observation period of 5 minutes has elapsed. Patients can if necessary be re-treated with their assigned treatment during this 5-minute TTH determination period, with up to 3 bottles Fibrocaps (3 g) in total.

Patients who do not achieve hemostasis within 5 minutes, are to be considered as failed, and are treated in the conventional way with treatment at the discretion of the surgeon, as long as the treatment does not contain thrombin.

Other bleeding sites (OBS) may be treated with Fibrocaps after hemostasis has been achieved at the TBS. However, all of the remaining Fibrocaps should not be used until after the 5-minute assessment period has elapsed in order to ensure that adequate Fibrocaps is available to use in the event of re-bleeding from the TBS.

Study burden and risks

Fibrocaps is made from human blood, therefore it may carry risk of transmitting infectious agents. The risk of transmitting infectious agents cannot be completely ruled out, because products made up of human blood may have unknown viruses and other infectious agents that can cause disease.
Subjects who test positive for antibodies to thrombin or subjects who have abnormal excessive bleeding, which might be suggestive of an immune response to fibrinogen, may also have their samples tested for antibodies to the fibrinogen in Fibrocaps. The development of a mild immune response (low levels of antibodies) to thrombin has been seen in several patients treated with Fibrocaps. Currently no patient safety concerns have been linked to these test results. None of the patients treated with Fibrocaps or other related products have experienced abnormal excessive bleeding or any other symptoms of an immune response to fibrinogen.
Signs and symptoms of allergic reactions may include but are not limited to: burning and stinging at the application site, hives, difficulty in breathing, chills, flushing, headache, low blood pressure, lethargy (sluggishness), rapid heartbeats, tightness of the chest, tingling, vomiting and wheezing. Other side effects that have been reported for fibrin sealants include: blood clots in veins or arteries where the drug was unintentionally applied inside the blood vessels, nausea, fever, bleeding, and irregular heartbeats. Medication to treat a potential allergic reaction will be available in the hospital.
A blood clot can occur in veins or lungs when a fibrin sealant is unintentionally applied directly into a blood vessel. Larger blood clots may cause medical problems, dependent on where they are found in the body. The most serious problems may occur when a blood clot ends up in the lungs, which may lead to pain in the chest and/or breathing problems, or a blood clot in the brains, which may result in a change in speaking, thinking or moving. Another operation may then be necessary.
In the rare case that the symptoms are serious, it may be necessary to remove the adhesions by means of an operation. The physician treating you can discuss this with you in more detail.
As with any medicine, side effects may occur during this study. All side effects or changes in your health need to be mentioned to study personnel.
Fibrocaps has not been tested in pregnant women. If the patient becomes pregnant while participating in this research study, it is important that she

notifies the study surgeon immediately. The study surgeon will ask for permission to follow the progression and outcome of the pregnancy, to ensure the research study procedures have no bad effects on the patient health or the baby*s health.
Possible benefits of using Fibrocaps during surgery will be shortening the bleeding time of the surgery and thus decreasing post-operative complications.

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

Inclusion Criteria (pre-surgery):
1. Subject has signed an institutional review board/independent ethics committee (IRB/IEC)-approved informed consent document
2. Subject is undergoing one of the surgical procedures described above

3. Subject age is >=18 years at time of consent
4. If female and of child-bearing potential, subject has negative pregnancy test during screening and is not breast-feeding
5. If subject is a sexually active male or a sexually active female of child-bearing potential, subject agrees to use a medically accepted form of contraception from the time of consent to completion of all follow-up study visits;Inclusion Criteria (during surgery):;1. Subject has not received blood transfusion between screening and study treatment
2. Presence of mild or moderate bleeding/oozing when control by conventional surgical techniques, including but not limited to suture, ligature and cautery is ineffective or impractical
3. Absence of intra-operative complications other than bleeding which, in the opinion of the Investigator, may interfere with the assessment of efficacy or safety Confidential
4. No intra-operative use of a topical hemostat containing thrombin prior to study treatment
5. Approximate TBS surface area of <= 100 cm2

Exclusion criteria

Exclusion Criteria:
1. Subject has known antibodies or hypersensitivity to thrombin or other coagulation factors
2. Subject has history of heparin-induced thrombocytopenia (only for vascular subjects where heparin use is required)
3. Subject has known allergy to porcine gelatin
4. Subject is unwilling to receive blood products
5. Has any clinically-significant coagulation disorder that may interfere with the assessment of efficacy or pose a safety risk to the subject according to the Investigator, or baseline abnormalities of INR > 2.5 or aPTT > 100 seconds during screening that are not explained by current drug treatment (e.g., warfarin, heparin)
6. Aspartate Aminotransferase (ASAT/AST) or Alanine aminotransferase (ALAT/ALT) > 3 x upper limit normal range during screening, except for subjects undergoing liver resection surgery or with a diagnosis of liver metastases where there is no upper limit for these analytes due to the nature of their disease
7. Platelets < 100 x109 PLT/L during screening
8. Subject has medical, social or psychosocial factors that, in the opinion of the Investigator, could impact safety or compliance with study procedures
9. Subject is currently participating or has participated in another clinical study involving another investigational agent within 4 weeks of the planned date of surgery or is planning participation in another clinical trial within 4 weeks after surgery

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-08-2012
Enrollment:	180
Type:	Actual

Medical products/devices used

Generic name:	Fibrospray Delivery device
Registration:	No
Product type:	Medicine
Brand name:	Fibrocaps
Generic name:	Fibrin sealant

Ethics review

Approved WMO Date:	04-05-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-07-2012
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO	

Date:	12-11-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-12-2012
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-01-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	01-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	08-03-2013
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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
EudraCT	EUCTR2011-006174-47-NL
ClinicalTrials.gov	NCT01527357

Register	ID
CCMO	NL40295.042.12