A Phase 2 , Randomized , Single - Blind , Controlled , Comparative Efficacy and Safety Study of Topical Fibrocaps * and Gelatin Sponge in Surgical hemostasis in the Netherlands

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1. To characterize the efficacy of topical Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, in surgical subjects when control of mild to moderate bleeding by standard surgical techniques is ineffective and/or impractical2. To...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Hepatobiliary therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON36279

Source
ToetsingOnline

Brief title
A phase 2 study of Fibrocaps in the Netherlands.

Condition

- Hepatobiliary therapeutic procedures

Synonym
Liver resection, Liver 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

The primary efficacy endpoint is mean Time to Haemostasis of Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone.

Secondary outcome

The secondary efficacy endpoints will be the proportion of subjects achieving hemostasis within 3, 5, and 10 minutes.

The safety and tolerability of Fibrocaps plus gelatin sponge USP and gelatin sponge USP alone will be characterized by the following safety parameters:

• Incidence and severity of treatment-emergent adverse events

• Incidence and grade of treatment-emergent clinical laboratory abnormalities

• Proportion of subjects developing anti-thrombin antibodies

Additional data related to the safety or activity of Fibrocaps will be collected and may be used in exploratory analyses. These may include: the dose of Fibrocaps per cm2, total surface area treated, post-operative drain fluid volume, use of alternative topical hemostatic agent(s) and use of blood products.

The safety and performance of the Fibrospray delivery device will also be characterized during this study by determining the incidence and severity of adverse events related to the device and the number of device failures or malfunctions. In addition, Investigators will formally assess the device and device performance following each surgery by completing the Fibrospray Device Assessment Form for each subject treated.

Study description

Background summary

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

Study objective

1. To characterize the efficacy of topical Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, in surgical subjects when control of mild to moderate bleeding by standard surgical techniques is ineffective and/or impractical
2. To characterize the safety of topical Fibrocaps plus gelatin sponge, as compared to gelatin sponge alone, in surgical subjects when control of mild to moderate bleeding by standard surgical techniques is ineffective and/or impractical

Study design

A multi-center, randomized, single-blind, controlled, comparative efficacy and safety trial in subjects undergoing hepatic resection. The study will enroll 60eligible subjects and be conducted at 5 sites in the Netherlands.
Subjects will provide written informed consent prior to undergoing any protocol-related assessments or procedures up to 30 days prior to surgery. Screening will take place up to 14 days prior to surgery and include recording of subject demographics, surgical history, medical history, and bleeding history; a physical examination including weight, vital signs, and clinical laboratory measures. On Day 1, subjects with mild or moderate bleeding during surgery that necessitates the use of an adjunct to hemostasis will be

randomized in a 2:1 ratio to Fibrocaps plus gelatin sponge (USP) [FCGS = active] or absorbable gelatin sponge (USP) alone [GS = control]. Subjects assigned to the FCGS group will be treated with topical Fibrocaps powder using the Fibrospray device followed by application of an absorbable gelatin sponge (USP) and light manual pressure with sterile gauze. Subjects assigned to GS will be treated only with an absorbable gelatin sponge (USP) followed by light manual pressure with sterile gauze.
A target bleeding site (TBS) with mild to moderate bleeding and a maximum surface area of approximately 100 cm2 will be identified, treated according to group assignment, and used to measure TTH. Up to one vial (1.5 g) of Fibrocaps will be applied to the TBS in the FCGS group, which is adequate to provide a thin layer of Fibrocaps powder over an area of approximately 100 - 150 cm2. The Fibrocaps should be applied quickly to the TBS, and typically completed within 30 seconds. Partially used vials should be removed from the device after inverting the device to clear the powder from the device and weighed to measure the dose of Fibrocaps applied to the TBS in each subject.
The measurement of TTH will begin (Tstart) at the time the Fibrocaps application to the TBS starts for the FCGS group and at the time the gelatin sponge is applied to the TBS in the GS group. Assessment of hemostasis will be made by carefully lifting the gauze and checking for bleeding through or around the gelatin sponge starting at 1 minute post Tstart and recur every 1 minute until hemostasis or 10 minutes has elapsed, whichever comes first.
As part of the dose exploration with Fibrocaps in this study, if hemostasis has not occurred within 3 minutes in the FCGS group, the surgeon may re-apply up to one additional vial (1.5 g) of Fibrocaps and continue to assess TTH every minute. If hemostasis has not been achieved within 10 minutes of Tstart in either group, the subject will be considered a treatment failure and the surgeon will implement additional hemostatic measures, including surgical interventions or the use of alternative topical hemostatic agents that do not contain thrombin.
Following the 10-minute observation period, in the FCGS group remaining unopened vials of Fibrocaps from the allotted quantity (3 vials of Fibrocaps per subject) may be used by the surgeon at sites other than the identified TBS that require an adjunct to hemostasis. The weight of Fibrocaps powder used to treat bleeding sites other than the TBS will be recorded.
Subjects will undergo follow-up safety evaluations after surgery on Day 1, and on Days 2, 7 and 29, which will consist of clinical and laboratory measures as indicated in the Schedule of Assessments (Appendix 1).
The presence of anti-thrombin antibodies in the plasma of study subjects who are treated in the study will be measured in plasma samples collected during screening and at the Day 29 visit.

Intervention

Each subject will be treated during a single surgical procedure on Day 1. Subjects will be randomized in a 2:1 manner within each site to one of the two treatment groups: FCGS and GS. The Fibrospray delivery device will be used to

rapidly apply (in <= 30 seconds) up to 1.5 g (1 vial) of Fibrocaps from a distance of approximately 5 cm to the TBS, which is followed by application of an absorbable gelatin sponge (USP) cut to appropriate size and light manual pressure with sterile gauze. Re-application of up to an additional 1.5 g of Fibrocaps at 3 minutes post Tstart is allowed for subjects in the FCGS group that have not achieved hemostasis.
Subjects in the GS group will be treated with an absorbable gelatin sponge (USP), cut to appropriate size, followed by light manual pressure with sterile gauze. Excess gelatin sponge should be removed from the bleeding site once hemostasis has been achieved.

Following the 10-minute observational period, remaining unopened vials of Fibrocaps from the allotted quantity (3 vials of Fibrocaps per subject) may be used by the surgeon at surgical bleeding sites other than the TBS that require an adjunct to hemostasis. Vials used to treat sites other than the TBS should be retained and accurately weighed. TTH is not measured.

Study burden and risks

Fibrocaps* is made from human blood; therefore, it may carry a risk of transmitting infectious agents. The risk of transmission of an infectious agent has been reduced by screening donors for prior exposure to certain viruses, by testing them for presence of certain current viral infections, and by the inactivation and removal of certain viruses. Despite all these preventive measures, such products may still potentially
transmit disease.
There is also the possibility that unknown infectious agents may be present in such products. As with any medicine, drug reactions may occur during treatment with fibrin sealant.
As with any medicine, drug reactions may occur during treatment with fibrin sealant, and all side effects need to be mentioned.
Allergic reactions, in rare cases, have been reported for other fibrin sealants. 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 (sluggish), nausea, restlessness, rapid heartbeats, tightness of the chest, tingling, vomiting and wheezing.
Blood clots in the veins and in the lungs may occur if the fibrin sealant is unintentionally applied into the blood vessel. Although it is very rare, a blood reaction to fibrin sealant components can occur. In addition, tissue adhesion at undesired sites may occur after application of fibrin sealant, if not applied correctly.
As with any experimental product, there may be unexpected side effects. The patient may experience the adverse reactions (unwanted events) listed above or none of these adverse reactions.
Fibrocaps* has not been tested in pregnant women. The medication or treatment used in this study may pose a risk to developing fetuses or to babies who are

being breastfed. If the patient becomes pregnant while participating in this study, it is important that she notifies the study doctor immediately. The study doctor will ask for permission to follow the progression and outcome of the pregnancy to ensure the study
procedures have no bad effects on the patient*s health or the baby*s health. Possible benefits of using Fibrocaps* during liver surgery will be shortening the bleeding time of the operated liver during 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

1 . Male or female aged >= 18 years
2 . Subjects who are able and willing to provide written and signed informed consent

3 . Willing to use a medically accepted form of contraception from the time of consent to completion of all follow - up study visits
4 . A life expectancy of at least one year;Intra-operative Inclusion Criteria
5 . Presence of mild or moderate bleeding and control by conventional surgical techniques including but not limited to suture , ligature , and cautery is ineffective or impractical
6 . Absence of intra - operative complications other than bleeding which , in the opinion of the Investigator , may interfere with the assessment of efficacy or safety
7. No intra-operative use of a topical hemostat containing thrombin
8. Target Bleeding Site surface area of less than approximately 100 cm2.

Exclusion criteria

1 . Pregnant or lactating women
2 . Has a known intolerance to blood products or components to Fibrocaps
3 . Unwilling to receive human blood products
4 . Subject has a known allergy to porcine gelatin
5 . A mental or physical condition that would , in the opinion of the Investigator , place the subject at an unacceptable risk or render the subject unable to meet the requirements of the protocol
6 . 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 during the 4 weeks after surgery
7 . 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
8 . Platelets < 100 x 10E9 PLT / L during screening
9 . aPTT > 100 seconds during screening
10 . INR > 2.5 during screening

Study design

Design

Study phase:	2
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):	07-01-2011
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	FibroSpray delivery device
Registration:	No
Product type:	Medicine
Brand name:	Fibrocaps
Generic name:	Fibrin sealant (fibrinogen and thrombin)

Ethics review

Approved WMO Date:	08-10-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-11-2010
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-12-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-04-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-06-2011
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	EUCTR2010-020202-16-NL
CCMO	NL33102.042.10