A Prospective, Randomized, Double-Blind, Multicenter Clinical Trial to Evaluate the Safety and Efficacy of the Z-Lig Medical Device Compared to Allograft for the Reconstruction of Ruptured Anterior Cruciate Ligaments

Published: 08-03-2011
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The purpose of this clinical trial is to demonstrate the safety and efficacy of the Z-Lig* device for the treatment of ruptured ACL of the knee compared to allograft.

Ethical review	Approved WMO
Status	Pending
Health condition type	Tendon, ligament and cartilage disorders
Study type	Interventional

Summary

ID

NL-OMON38288

Source
ToetsingOnline

Brief title
Z-Lig study

Condition

- Tendon, ligament and cartilage disorders

Synonym
ruptured anterior cruciate ligament

Research involving
Human

Sponsors and support

Primary sponsor: Aperion Biologics Inc.
Source(s) of monetary or material Support: Aperion Biologics;Inc.

Intervention

Keyword: ACL reconstruction, allograft, anterior cruciate ligament, xenograft

Outcome measures

Primary outcome

Primary performance endpoint:

• KT-1000 (2000) knee laxity (Maximum side to side difference reported in mm

injured vs. non-injured
• Pivot Shift Tests and

• Lachman*s Test

Primary efficacy endpoint: KT-1000 (2000) Knee laxity (Maximum side to side

difference reported in mm injured vs. non-injured

The safety endpoints of this Trial are:

• Incidence of Adverse Events

• Incidence of Adverse Device Effects

• Incidence of Serious Adverse Events

• Incidence of Serious Adverse Device Effects

Secondary outcome

The secondary endpoints of this Trial are:

KT-1000 or 2000

• Value at each time point

IKDC Knee Examination

• Anterior drawer test

• Lachman*s test

• Pivot Shift

• Effusion

IKDC Subjective Knee Evaluation

• Pain

• Function

• SF-36 Health Survey

• Tegner Activity Level Scale

Global Subject Satisfaction

X-ray evaluation of tunnel position and diameter:

• Anteroposterior (AP)

• Posteroanterior (PA)

• Rosenberg Flexion

• Lateral

Magnetic Resonance Imaging (MRI) evaluating biological changes:

• Graft ligamentization

• Graft failure

• Osteitis with tunnel widening

• Synovitis

• Other internal derangement such as meniscal tears and articular cartilage

injury

The tertiary endpoints of this Trial are:

• Healthcare Utilization and Costs

• Return to Work

Study description

Background summary

The anterior cruciate ligament (ACL) is the key stabilizer of the knee joint and is frequently injured in athletic activities. More than 800,000 patients with damaged ACLs undergo in-patient or out-patient surgical intervention globally each year. Current surgical techniques consist of either the use of the patient*s own tissue to reconstruct the ACL (autologous harvest procedures) or, less frequently, cadaveric tissue grafts (allografts).
All grafting techniques have disadvantages and risks. Reconstruction utilizing an autologous harvest procedure involves two surgical sites, the primary operative site and the additional harvest site. The harvest procedure for reconstruction often results in larger or additional incisions, increased pain, longer recovery periods and increased morbidity. Cadaveric tissue allografts offer a limited source of ACL replacement tissue due to the scarcity of available tissue from young healthy donors. . Variability in tissue quality and performance is also an issue between donors. The perceived risk of transmission of hepatitis and other diseases has been another obstacle to the acceptance of cadaveric tissue.
In an effort to overcome the limitations of both autologous and cadaveric allograft materials, the use of synthetic and animal-derived tissues has been investigated. To date, these investigations have led to failure, and there are currently no effective synthetic materials or animal tissue substitutes

available for widespread use in ACL reconstruction.

Study objective

The purpose of this clinical trial is to demonstrate the safety and efficacy of the Z-Lig* device for the treatment of ruptured ACL of the knee compared to allograft.

Study design

This is a multicenter, double-blind, randomised clinical investigation that will be performed in up to 8 centers. A maximum of 66 patients will be included. The study will last 2 years for the allograft patients and 5 years for the Z-Lig patients.

Intervention

50% of the patients will be treated with the Z-Lig device, the remaining patients will be treated with an allograft.

Study burden and risks

Complications of arthroscopic knee surgery include infection, swelling, and blood clots in the leg. Complications are unusual after knee arthroscopy, and while they are cause for concern, knee arthroscopy is considered a low-risk surgical procedure.

Side-effects of general anaesthesia are feeling sick and vomiting after surgery, shivering, sore throat, headache, feeling tired and confused for a couple of days. Serious complications are extremely rare. They include:nerve damage, damage to teeth, lips or tongue, allergic reactions.

Risks and side effects related to the Z-Lig as reported from a US Investigational Device Exemption, single center study include the following: Bruising with discoloration, Blood Urea Nitrogen (BUN) elevation, Baker*s cyst, Decreased hematocrit & hemoglobin induced by Vioxx®, Fever, General malaise, Graft rupture/failure, Knee laxity, Knee/tibia swelling with effusion, Limited knee range of motion, Local incision suture reaction, Muscle injury/damage, Nerve injury/damage, Pain, Redness, Superficial or deep wound infection, Surgical knee scar, Synovitis (inflammation of synovial membrane).

Risks related to radiology include the following: Minimal radiation exposure

Allergic Responses to the the Z-Lig may include the following:

A total body (systemic) response with associated hives (skin becomes red and itchy), Shortness of breath, Fainting, Local tissue response (inflammation) at the surgical site

Risks involving porcine xenograft tissue include the following:

The Z-Lig is manufactured from porcine (pig) xenograft. There is a risk you may be sensitive to this product.
The Z-Lig is manufactured and packaged under aseptic conditions and additional testing is performed throughout the manufacturing process to ensure the material is free from any infectious agents.

Risks related to the allograft include the following:

Despite rules and regulations for tissue banks regarding processing and procedures of human tissue, there is still a small potential risk of disease transmission from using allograft (cadaver) tissue. The tissue bank will make every effort to eliminate this possibility.

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. Potential Subject is able to provide informed consent and must sign the EC-approved Informed Consent Form,
2. Male or female between the ages of 18-60 years,
3. Skeletally mature as evidenced by closure of the epiphyseal plate on x-ray,
4. Simple ACL insufficiency with no concurrent multi-axial or multi-ligament instabilities or knee dislocations,
5. Diagnosed with an acute or chronic primary ruptured anterior cruciate ligament of the knee documented by:
a) physical exam with positive Lachman*s test or,
b) *5 mm side-to-side difference by KT 1000 (or 2000), 10-20 lb force or,
c) MRI of the affected knee
6. Acute injuries must not exhibit effusion or inflammation,,
7. Pre-Injury Tegner Activity Score <8,
8. If female, for the first 12 months post operative, actively practicing a contraception method, or practicing abstinence, or surgically sterilized, or postmenopausal,
Applicable to Denmark only:
9(a): Fertile women those are not pregnant as demonstrated by a negative pregnancy test at the baseline and prior to surgery and use safe method of contraception. Acceptable contraception methods include: intrauterine devices and hormonal contraceptives (contraceptive pills, implants, transdermal patches, hormonal vaginal devices, injections with prolonged release).;9(b): Sterilized or infertile Subjects are exempt from the requirement to use contraception. Subjects must have undergone surgical sterilization (hysterectomy or bilateral ovariectomy) or be postmenopausal defined as 12 months or more with no menses prior to enrollment).
9. The contralateral knee is asymptomatic, stable and fully functional,
10. Must be physically and mentally willing and able to comply with post-operative rehabilitation and routinely scheduled clinical, radiographic and rehabilitation follow up visits through 24 months,
11. Osteoarthritis of Grade II-III acceptable based on the ICRS scale (no Grade IV prior to baseline) if the treatment does not impact the ACL rehabilitation protocol
12. Subjects requiring a meniscal repair without modification to the rehabilitation protocol.

Exclusion criteria

1. Pregnant based on a positive hCG serum or an in vitro diagnostic test result or breast-feeding,

2. Has osteoarthritis of Grade IV,
3. Require a menisectomy (>50%) or meniscal repairs where the treatment has an impact the ACL rehabilitation protocol,
4. Has inflammatory arthritis determined by history, examination or serology,
5. Has an active or latent infection of the affected knee joint or any other systemic infection currently under treatment or treated with antibiotics within the previous 3 months,
6. Has a history of alcoholism, medication, or intravenous drug abuse, psychosis, has a personality disorder(s), poor motivation, emotional or intellectual issues that would likely make the potential Subject unreliable for the Trial, or any combination of variables in the Principal Investigator*s judgment that would exclude a potential Subject,
7. Clinically documented acute or chronic disease, other than the indication to be treated in this Trial that might affect life expectancy, or make it difficult to interpret the potential Subject*s outcome according to the Protocol (i.e., renal, hepatic, cardiac, endocrine, hematologic, autoimmune, metabolic bone, crystal deposition, severe degenerative joint, neoplastic diseases),
8. Potential Subjects with a medical condition that interferes with their ability to participate in a standardized rehabilitation program,
9. Participated in any other investigational drug or device trial 60 days prior to screening visit or who will receive such a drug or device during the course of this Trial,
10. Any previous autograft or allograft revision ACL surgery to either knee,
11. Complete absence of the meniscus cartilage in the affected knee, documented by MRI,
12. Significant posterior cruciate ligament (PCL) or posterolateral corner ligament injury to the affected knee, documented by examination or MRI,
13. Potential Subjects with a known pork food sensitivity/allergy,
14. Has contraindications for MRI,
15. Has a neuromuscular, neurosensory, or musculoskeletal deficiency that limits the ability to perform objective functional assessment of either knee, such that a Subject experienced polytrauma and/or either lower extremity is immobilized to assess knee stability,
16. Potential Subject who is obese or above a Body Mass Index (BMI) of >40 (BMI =kg/m2). See Appendix D.
17. Treatment for any condition during the same procedure, such as an acute cartilage injury, that will modify the ACL rehabilitation protocol.
18. Subjects who plan to return to competitive sports activities within 9 months post surgery

Study design

Design

Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)

Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	15-02-2011
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Generic name:	the Z-Lig
Registration:	No

Ethics review

Approved WMO Date:	08-03-2011
Application type:	First submission
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	07-05-2012
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	13-12-2012
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	26-05-2014
Application type:	Amendment
Review commission:	METC Isala Klinieken (Zwolle)
Approved WMO Date:	21-08-2014
Application type:	Amendment

Review commission: METC Isala Klinieken (Zwolle)

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	NL34648.075.10