Prospective Post-Market Data Collection on Patients with Bone Marrow Lesions in the Knee Treated with Subchondroplasty procedure

Published: 20-02-2018
Last updated: 11-07-2024

Primary objective: To evaluate the performance of the SCP procedure in treatment of bone marrow lesion(s) (BML(s)).Secondary objective:Secondary objectives include documenting clinical outcomes such as pain, function of daily living, function of...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Bone disorders (excl congenital and fractures)
Study type	Interventional

Summary

ID

NL-OMON52931

Source
ToetsingOnline

Brief title
SCP-EMEA-01

Condition

- Bone disorders (excl congenital and fractures)

Synonym
Bone marrow lesion | Bone defect

Research involving
Human

Sponsors and support

Primary sponsor: Zimmer Biomet

Source(s) of monetary or material Support: De sponsor (Zimmer Biomet)

Intervention

Keyword: AccuFill Bone substitute material (BSM), Bone Marrow Lesion, Pain Relief, Subchondroplasty Procedure

Outcome measures

Primary outcome

Knee Injury and Osteoarthritis Outcome Score (KOOS) Pain Subscale:

KOOS is a validated instrument which measures knee pain and function using five subscales: pain, symptoms, function in daily living, function in sport and recreation, and quality of life. The instrument consists of 42 standardized questions each having 5 point Likert response scale.

Secondary outcome

Knee Injury and Osteoarthritis Outcome Score (KOOS):

KOOS is a validated instrument which measures knee pain and function using five subscales: pain, symptoms, function in daily living, function in sport and recreation, and quality of life. The instrument consists of 42 standardized questions each having 5 point Likert response scale.

EuroQol-5 Dimensions (EQ-5D):

The EQ-5D is a validated instrument that assesses an individual*s current health status and heath related quality of life. The EQ-5D-5L descriptive component assesses five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression over five levels of severity.

Numeric Rating Scale (NRS) for pain:

The NRS is a validated measure of knee pain. The NRS is an 11 point Likert type scale anchored by 0 *no pain* and 10 *worst possible pain*. Subjects rate their average pain over the last week.

Heathcare Utilization:

Health economics will be evaluated throughout the study. Healthcare utilization for each subject will be recorded to capture information about their use of healthcare resources following study treatment and follow-up.

Subject Global Satisfaction Scale:

The subject global satisfaction is concerned with determining patient-related factors such as patients* satisfaction with treatment, and experienced health outcomes. Patient preferences will be measured utilizing questions to elicit patient satisfaction following a SCP Procedure within the study.

Knee Radiograph

A long standing anterior-posterior (AP) fixed flexion radiograph of the index knee is acquired. Alignment and K-L grade will be measured according to validated, prospectively defined techniques described in signed charters produced by the Imaging Core Laboratory. This charter will specify radiograph acquisition details, transfer, and analysis techniques. All X-rays will be transferred to the Imaging Core Laboratory for independent re-view. Radiographs will be taken for a subset of subjects only at baseline and

at the 12 Month Follow-up Visit.

Magnetic Resonance Imaging (MRI)

MRI will be used to determine eligibility for all subjects. Diagnosis of BML*s have to be established utilizing fat suppressed MRI images (e.g. T2FS).

For a subset of subjects the MRI will be obtained according to validated, prospectively defined techniques as described in the Image Acquisition Protocol and Image Review Charter produced by the Imaging Core Laboratory. These charters will specify MRI acquisition details, transfer, and analysis techniques. All MRI will be transferred to the Imaging Core Laboratory for independent review. MRIs will be taken at the time of screening or baseline and at the 12 Month Follow-up Visit for the first 45 patients and at screening and 24 month follow-up for the following 50 patients.

Adverse Events (AEs)

AE forms will document a description of the AE, onset and resolution dates, severity, seriousness, treatment, and relatedness to the device and the procedure. It will also document whether the event was anticipated or unanticipated.

Reoperation/revision:

Incidence and time from initial SCP Procedure to re-operations and revisions in index knee will be recorded at study exit.

Study description

Background summary

Subchondral bone defects, sometimes called bone marrow lesions (BMLs), are MRI-visible defects that can be seen on fat-suppressed MRI sequences, where they appear as a hazy white area against the background of darker bone. Pathologists have shown that BMLs represent a healing response to trauma such as micro trabecular fractures of the subchondral bone. BML defects have been highly correlated with pain symptoms in the knee. However, BMLs and their impact on knee pain and function went relatively unrecognized in the orthopedic literature until 2011.

Treatment options for BMLs have been limited in the past. For degenerative or chronic BMLs, treatments have included core decompression, extracorporal shock wave therapy and pharmaceuticals. While core decompression seeks to directly stimulate the bone through a surgical procedure, it does not fill the voids and defects in the bone and is not widely used to treat BMLs in the knee. Subchondroplasty (SCP) is a procedure first described in 2007 to fill subchondral osseous defects associated with BMLs using an injectable bone substitute material (BSM), AccuFill. AccuFill is an injectable, self-setting, macro-porous, osteo-conductive, calcium phosphate bone graft substitute material that is intended for use to fill bony voids or gaps of the skeletal system of the extremities, spine, and the pelvis that are not intrinsic to the stability of the bony structure. These defects may be surgically created osseous defects, or osseous defects created from traumatic injury to the bone. AccuFill is a bone graft substitute that resorbs and is replaced with new bone during the healing process. AccuFill has unique properties that allow it to flow through the osseous defects in trabecular bone and then set up hard at body temperature. Two year results from a clinical study on 66 subjects considering total knee arthroplasty (TKA) has shown improvements in subject reported pain and function with only 30% of subjects undergoing revision to TKA at 2 years.

Preclinical studies in established animal models were used to evaluate safety of AccuFill for treatment of bone defects. A rabbit bilateral lateral femoral condyle defect model (4.8 mm diameter x 6 mm length cylindrical defect) through 24 weeks demonstrated that AccuFill caused bone induction and osteointegration at the implant sites, and was well tolerated. No significant Adverse Events (AEs) or indications of infections or rejections of the AccuFill material were observed in the preclinical evaluations of AccuFill. Studies demonstrated bone induction, osteointegration and potential for use as a bone void filler.

Davis, et al. presented a retrospective review of 50 subjects with a mean follow-up of 14.6 months after the SCP Procedure for BMLs in the knee.

Eighty-eight percent (88%) of subjects reported improvement in pain and 72% reported improvement in pain free walking distance. Four (4) subjects (8%) were revised to TKA.
Another retrospective study evaluated the effectiveness of the SCP Procedure in treating osseous defects in subjects reporting pain with documented BMLs associated with advanced knee OA. Data were collected from a consecutive subject series (N=66) who underwent the SCP Procedure combined with arthroscopy, performed at a single center by one surgeon. The study reported significant improvements in both pain and function, as measured by the Visual Analog Scale (VAS) and the International Knee Documentation Committee (IKDC) Subjective Knee Evaluation Form, through 2 years post-operative follow-up. Given that arthroscopic debridement alone has been previously shown to yield insignificant pain relief beyond 6 months post-op, the results suggest that SCP the Procedure is a promising approach for the treatment of osseous defects associated with BMLs in subjects with knee OA.
An observational cohort follow-up study (NCT01621893) is ongoing in the United States. The goal of this prospective, multi-center patient outcome observational cohort study is to document the short- and long-term safety and effectiveness of the SCP Procedure. In addition, a single-blind, randomized clinical study (NCT02905240) is recently initiated in the United States. A total of 201 patients will be enrolled. The primary objective of this RCT is to demonstrate superiority of the SCP Procedure with arthroscopy compared to arthroscopy alone for treatment of BMLs in the knee.

In addition, several other studies are ongoing to evaluate the clinical outcomes of the SCP Procedure.

Despite the growing interest in BML in multiple pathological conditions, demonstration of the clinical impact and treatment is lacking. The design of this study is intended to harness detailed patient demographic information (e.g., age, gender, location of defect, severity of symptoms, etc.) to determine the most suitable SCP procedure patient population in Europe. This study will also document the long-term, real-world evidence on the application of the SCP procedure in treatment of BMLs in the knee and associated symptoms.

Study objective

Primary objective:
To evaluate the performance of the SCP procedure in treatment of bone marrow lesion(s) (BML(s)).

Secondary objective:
Secondary objectives include documenting clinical outcomes such as pain, function of daily living, function of sports and recreation, and other knee related quality of life measures following a SCP procedure.
Other secondary objectives include evaluating subject global satisfaction, healthcare resource utilization and the safety profile by determining AEs,

surgical complications occurring from the time of surgery and the incidence and time to subsequent secondary surgical intervention including re-operation and revision.
For all 95 consecutive subjects at selected centers, X-ray and magnetic resonance image (MRI) variables will be evaluated.

Study design

This is a prospective, multi-center, post-market data collection study intended to collect data on the short- and long-term safety and performance of the SCP procedure.

Screening will consist of meeting all inclusion and exclusion criteria. A screening MRI to determine if the patients are eligible may be obtained up to 90 days prior to the study treatment. Subjects will provide demographic and medication history information. Within 2 months of the screening visit, subjects will return to the clinic for the study treatment.

Follow-up assessments will be conducted at 1 month, 3, 6, 12-months and annually up to 5 years post injection; all subjects will complete NRS, KOOS, EQ-5D, subject global satisfaction scale and healthcare utilization questionnaires. The investigative center will complete the follow-up form and collect information on treatment and knee related AEs. Follow-up assessments up to the 12-month visit will be preferably completed during an office visit. All annual follow-up assessments may consist of a structured telephone interview, electronic self-report or an office visit.

For a subset of approximately 45 consecutive subjects at selected centers, a long standing X-ray at baseline and 12 months follow-up (for the next 50 patients, at 24 months follow-up) visit and an MRI3 at screening or baseline (if screening MRI was not performed according to the Image Acquisition Protocol and Image Review Charter by Imaging Core Laboratory) will be obtained. All images will be transferred to the Imaging Core Laboratory for independent review. Image acquisition, transfer, and analysis procedures will be performed using validated, prospectively defined methods.

Intervention

Subchondroplasty (SCP) to fill subchondral osseous defects associated with BMLs using an injectable bone substitute material (BSM), AccuFill.

Study burden and risks

Benefits
The potential benefits of participation in the study are related to clinical outcomes associated with the SCP procedure for treatment of BMLs in the knee.

These clinical outcomes include relief of pain in the knee and improved function of the knee. In addition, the study in general could provide useful information for the future that may help medical doctors and investigators come up with an improved treatment plan for BML(s) in the knee.

Risks

Arthroscopy Procedure

Risks of surgical intervention include those risks currently associated with arthroscopic surgical interventions in the knee. These risks include intra-articular adhesions (scar tissue), superficial and/or deep wound infection, nausea and/or vomiting, bleeding, knee pain, muscle weakness, and postoperative blood clot (hematoma). Meniscal tear and plica formation (inflammation and thickening of a fold in the lining of the knee joint) may occur. There are possibilities of wound re-opening, deep vein thrombosis (blood clot), pulmonary embolus (lung clot), vascular or nerve injury and an allergic response to the anesthetic or medications. These risks are not unique to this study and may occur with any surgical intervention (arthroscopy procedure). Study subjects will be monitored post-operatively to assess the surgical site for any acute and chronic adverse reactions to ensure proper medical treatment can be administered.

Local Anesthesia

Some additional risks related to local anesthesia are swelling, pain, bleeding, bruising, nerve pain and loss of sensation in the skin and ligament around the knee.

Subchondroplasty

The most common risk associated with this procedure is significant pain in the operative area approximately 48 - 72 hours after the SCP procedure. Risks associated with subchondral implantation of AccuFill may also include tissue thinning over implant site, tenderness, redness, edema, seroma, hematoma, infection, swelling, fluid collection, loss of contour. Migration, extrusion, dehiscence, fracture and sloughing of AccuFill can occur as a result of excessive trauma. Neurovascular injury may occur due to surgical trauma. To minimize risks an experienced orthopedic surgeon will participate as your study doctor and will have well trained staff to perform the study procedures including post-operative rehabilitation.

X-ray

There will be exposure to radiation from the X-rays that need to be taken. The radiation used during the study may lead to damage to your health. However, this risk is small.

MRI

The magnetic field used by MRI scanners may cause implanted medical devices that contain metal to malfunction or heat up during the exam. Any loose metal object may cause damage or injury if it gets pulled toward the magnet. Dyes from tattoos can cause skin irritation. Medication patches can cause skin burns. Prolonged exposure to radio waves during the scan could lead to slight warming of the body. Patients may have some anxiety due to being in a confined space. The MRI technician will direct patients to reduce the possibility of

these risks. Questionnaires
There is a risk of being uncomfortable answering questions. While completing the questionnaires, you may tell the study staff that you feel uncomfortable or do not wish to answer a particular question.
Confidentiality
There is a risk of loss of confidentiality.
Other Risks
There may be unforeseen risks that we cannot predict.
We ask that you report to the doctor any illnesses or change in your health, even if you do not think it is related to the SCP Procedure. We will inform you as soon as possible about any new information relating to the procedures involved in this study.

Contacts

Public
Zimmer Biomet

Toermalijnring 600
Dordrecht 3316LC
NL
Scientific
Zimmer Biomet

Toermalijnring 600
Dordrecht 3316LC
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- At least 18 years of age at time of screening
- Patient with BML(s) in one or both knees, as diagnosed by the treating physician, willing and eligible to undergo the SCP procedure
- One or more BML(s) of the tibial plateau and/or femoral condyle extending to the ar-ticular surface of the joint confirmed on T2 weighted fat-suppressed or Proton Density MR Imaging by presence of white signal
- Index knee alignment is defined radiographically as one of the following: Neutral, <= 6° mechanical varus, or <= 6° mechanical valgus
- A KOOS Pain subscale total score < 70
- Is refractory to conservative non-surgical management of BML:
- having failed 2 or more of the following: hyaluronic acid (HA) injection, corti-costeroid injection, non-steroidal anti-inflammatory drugs (NSAIDs), physical therapy, bracing, or minimal surgical intervention (e.g. arthroscopy, debride-ment/chondroplasty, and/or loose body removal)
- and diagnosis of BML is >= 3 months of the study treatment
- Willing and able to comply with the study procedures
- Signed an informed consent form approved by Independent Ethics Committee (IEC)

Exclusion criteria

- Existing acute or chronic infections at the surgical site
- Bone in the index knee is non-viable or not capable of supporting and anchoring the implant
- Known systemic disorders or any systemic inflammatory condition (e.g. rheumatoid arthritis)
- Acute traumatic injuries with open wounds close to the bone defect which are likely to become infected
- Known metabolic bone disease, including disorders in calcium metabolism
- Known immunologic abnormalities, including inflammatory bone disease
- Has a history of any invasive malignancy (except non-melanoma skin cancer), unless treated with curative intent and with no clinical signs or symptoms of the malignancy for 5 years
- Diagnosis of patella-femoral joint osteoarthritis (OA) and/or primarily patella-femoral symptoms
- BML caused by acute trauma less than 3 months prior to enrollment
- Clinical and/or radiographic disease diagnosis of the index knee that includes any of the following:
- Kellgren-Lawrence grade 4 OA1
- BML located at anterior cruciate ligament (ACL)/ posterior cruciate ligament (PCL) insertion
- Any major or cartilage repair or alignment surgery (i.e. osteotomy,

autograft, scaffold, marrow stimulation, , all cell-based therapies, etc.) of the index knee within 12 months prior to enrollment
- Pregnant at time of injection
- Lactating at time of injection
- Use of any investigational drug or device within 30 days prior to enrollment
- Use of any investigational biologics within 30 days prior to enrollment

Study design

Design

Study type: Interventional

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	29-03-2018
Enrollment:	40
Type:	Actual

Medical products/devices used

Generic name:	AccuFill Bone Substitute
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	20-02-2018
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	30-10-2019

Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	14-07-2021
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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	NL62987.068.17