A Single-Center, Single-Cohort Study of FF-37101 for Bone Formation in the Maxillomandibular Region

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The primary performance objective is to demonstrate bone formation assessed based on bone height measurements, in the maxillomandibular region after filling extraction sockets with FF-37101. Secondary and exploratory performance objectives of this...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Bone and joint therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON55475

Source
ToetsingOnline

Brief title
A study with a bonefiller to stimulate bone formation in the jaw

Condition

- Bone and joint therapeutic procedures

Synonym
Bone formation, bone lesion

Research involving
Human

Sponsors and support

Primary sponsor: FUJIFILM Manufacturing Europe BV
Source(s) of monetary or material Support: FUJIFILM Manufacturing Europe BV

Intervention

Keyword: Bone filler, Bone formation, FF-37101, Jaw

Outcome measures

Primary outcome

The primary performance endpoint will be the proportion of patients that has bone formation in the grafted site after 6 months, as identified by CBCT imaging, will be 50% or more.

Secondary outcome

The secondary performance endpoint is the evidence of newly formed bone and its individual components, bone maturity, and soft tissue/marrow space, at 6 months post-treatment, identified by histologic analysis of biopsies of the pre-molar and molar teeth.

The exploratory performance endpoints are:

- The amount of bone that has been formed in the extraction socket assessed based on bone height measurements, at 3 months post-treatment, identified by cone beam computed tomography (CBCT) evaluation.
- The amount of FF-37101 at 6 months post-treatment, identified by histologic analysis of biopsies of the pre-molar and molar teeth.
- The implant stability quotient (ISQ) that is measured after placing the implant, identified by ISQ measurement devices.
- The bone volume that has been formed in the extraction socket at 3 and 6 months post-treatment, identified by CBCT evaluation.

Exploratory safety endpoint:

The safety objectives of this study are to assess the safety of the device, by assessing the overall incidence of device related serious adverse events.

Furthermore, the immunogenicity of R-collagen will be assessed by the detection of anti-device antibodies to R-collagen. Immunogenicity responses that show related clinical symptoms will be further investigated as part of the safety evaluation.

Study description

Background summary

Extraction of a tooth is generally indicated when a tooth cannot be restored or maintained in acceptable conditions for long term health, function, and/or esthetics. Tooth loss may have a direct impact on quality of life by impairing the ability to speak, masticate, and in some instances, socialize. In addition, the absence of a tooth triggers a cascade of biological events that typically result in significant local anatomic changes. It is well known that after tooth extraction, jawbone having supported the tooth undergoes significant reduction. The severe reduction in the size of jawbone negatively affects the prosthetic treatment, such as fixed bridge, removable denture and dental implant.

FUJIFILM has developed a new oral bone graft material, FF-37101, which intends to support new bone formation in the maxillomandibular region, including bone formation in the tooth extraction socket, sinus lift, periodontal defects, and other indications. FF-37101 is composed of sponge like granules that are manufactured from recombinant collagen (R-collagen) specifically designed for this product. On implantation, it is theorized that the FF-37101 pores act to absorb blood and form and stabilize the clot. The collagen sponge acts as a scaffold for new bone formation. Once placed in the bone defect area such as the tooth extraction socket, FF-37101 is gradually resorbed by the body*s natural enzymes, while new bone formation occurs within and along the surface of the FF-37101. The material is intended to be completely absorbed after implantation with replacement by new bone.

Preclinical testing has shown the potential of the investigational device for its intended use in humans. However, no clinical studies have been performed on FF-37101 to date, nor are there any equivalent products available on the market

to establish the safety and performance of FF-37101 in humans. In order to prove the safety and performance of FF-37101 in healthy adult subjects for bone formation in the maxillomandibular region, this study will be conducted. FUJIFILM has chosen socket preservation as a suitable method for determining the performance of FF-37101 for bone formation in the maxillomandibular region.

Study objective

The primary performance objective is to demonstrate bone formation assessed based on bone height measurements, in the maxillomandibular region after filling extraction sockets with FF-37101.
Secondary and exploratory performance objectives of this study are:
• To evaluate bone maturity and bone formation at 6 months post-treatment.
• To evaluate bone formation assessed based on bone height measurements, in the grafted site after filling of extraction sockets with FF-37101 at 3 months post-treatment.
• To evaluate FF-37101 resorption in the extraction socket at 6 months after FF-37101 implantation.
• To evaluate primary implant stability of the implant placed at 6 months post-treatment.
• To evaluate bone formation assessed based on bone volume measurements, in the grafted site after filling of extraction sockets with FF-37101 at 3 and 6 months post-treatment.

The safety objectives of this study are to assess the safety of the device by assessing the overall incidence of serious adverse device effects.

Study design

This is a single-center, single cohort, non-randomized, open-label study of FF-37101 following the extraction of a hopeless tooth (front, pre-molar or molar) to demonstrate the safety and performance of the FF-37101 device in adult subjects.

All subjects included in the study and that fulfill the inclusion and exclusion criteria will be treated with FF-37101. No comparator or other treatments will be used in this clinical investigation. Subjects will be followed up for 6 months.

Intervention

The tooth extraction will be completed according to standard of care. The extraction socket will be thoroughly curetted and irrigated with a sterile 0.9% saline solution. A buccal dehiscence will be examined clinically using periodontal probe and explorer immediately after extraction and the buccal bone loss will be recorded in mm. FF-37101 will swell when it comes into contact

with blood or saline. FF-37101 will be pre-soaked with sterile 0.9% saline solution or the subject*s blood before the implantation. After the pre-soaking, the extraction socket will then be filled with FF-37101. FF-37101 granules in the socket will be gently compressed to fill to the soft tissue edge. Caution will be used not to over pack FF-37101 into the socket and avoid granule fragmentation. The wound is closed using sutures. If possible, no membrane will be utilized during or following placement of FF-37101. The decision of the use of a membrane will be up to the investigator for the success of the surgery.

Study burden and risks

The subjects are expected to visit the clinic for an initial screening visit. Subsequently, during visit 1 the actual tooth extraction and FF-37101 implantation are performed and afterwards 5 follow up visits (2-6) and an intermediate telephone contact will be scheduled. During all visits and the intermediate telephone contact, safety of the FF-37101 device will be evaluated.

At visit 1, 5 and 6 a cone beam computed tomography (CBCT) will be taken. A CBCT-scan uses X-rays. The total radiation exposure is will be about 00.0075 mSv (0.0025 mSv for each scan). For comparison: the background radiation in the Netherlands is ~2,5 mSv each year.

At visit 6 a biopsy is taken for subjects treated for pre-molar and molar teeth.

Blood (7 ml) will be drawn for immunogenicity testing during visit 1, 4, 5 and 6. If immunogenicity testing results are available and classified as positive, subjects will be asked to provide an extra blood sample and to conduct an extra phone contact visit. Subjects shall be informed that the extra blood sample and phone contact visit are additional and that they are free to reject participation.

Based on all preclinical testing, the Sponsor anticipates the following adverse device effects:
• Allergic reaction to R-collagen/FF-37101.
• Superficial wound infection.
• Deep wound infection.
• Loss or migration of the graft material.

Participation in this research will have the following benefits for the subject:
- Potential improved healing and bone formation, to facilitate further treatment for dental restoration, such as prosthetic treatment.
- state-of-the-art diagnostic examinations
- partial reimbursement of dental treatments, until placement of the first part of the implant

The sponsor believes that any potential risk presented by this investigation has been minimized and that adequate testing, safeguards, and safety monitoring have been incorporated into the investigation to further minimize and mitigate the risks. FUJIFILM Manufacturing Europe BV firmly believes that the benefits of FF-37101 outweigh the potential risks posed to participating subjects.

Contacts

Public
FUJIFILM Manufacturing Europe BV

Oudenstaart 1 1
Tilburg 5000 LJ
NL
Scientific
FUJIFILM Manufacturing Europe BV

Oudenstaart 1 1
Tilburg 5000 LJ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- 18 year or older at time of informed consent.
- Have 1 tooth (front, pre-molar or molar) of poor prognosis diagnosed for tooth extraction
- Have 1 or more healthy tooth/teeth immediately adjacent to the tooth that is to be extracted

- Have a type I or type II socket of the buccal alveolar bone of the tooth to be extracted
- Absence of pockets of 5mm or more in the full dentition, with exception of the pocket of the tooth to be extracted.
- Able to return for follow-up visits, as defined in this clinical investigation plan, after tooth extraction.
- Scheduled to have an implant placed 6 months after tooth extraction and FF-37101 implantation

Exclusion criteria

- Signs of active inflammation, i.e. presence of inflammatory fluid during tooth extraction
- Active generalized periodontal disease; evident periapical radiolucencies or abscesses;
autoimmune disorders; taking or having a history of bisphosphonate medications or Denosumab
(history of MRONJ (medication-related osteonecrosis of the jaw)/BRONJ (bisphosphonate-related
osteonecrosis of the jaw)); congenital or metabolic bone disorders; or uncontrolled diabetes.
- Metal root pin or dental implant completed on any tooth adjacent to the tooth to be extracted in this
clinical investigation
- Current or former smoker or user of chewing tobacco or nicotine-containing products. Former
smokers or users are defined as subjects who smoked 10 cigarettes or more (or an equivalent
amount of other tobacco products) per day in the 5 years prior to screening
- Females who are pregnant, breastfeeding, or are planning to conceive during their enrollment in
the clinical investigation
- History of any clinically significant mental and/or psychological, or other major disease, as
determined by the investigator that would prevent dental treatment.
- Inability to effectively communicate with study staff during the clinical investigation.
- History of any severe allergic or anaphylactic reactions to collagen or gelatin, or current sensitivity
to collagen or gelatin
- Unwillingness or inability to comply with the requirements of the clinical investigation plan
- Previous head and neck radiation- or chemo- therapy
- Other reasons that, in the opinion of the investigator, will make the subject unsuitable for

enrolment

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-09-2020
Enrollment:	30
Type:	Actual

Medical products/devices used

Generic name:	FF-37101
Registration:	No

Ethics review

Approved WMO Date:	18-09-2019
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	26-02-2020
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-11-2020

Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	11-10-2021
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	07-02-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 24676
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL65005.028.19
Other	NL8363
OMON	NL-OMON24676

Study results

Date completed:	04-09-2023
Actual enrolment:	28