Randomized Controlled Study of a Local Osteo-Enhancement Procedure (LOEP) to Prevent Secondary Hip Fractures in Osteoporotic Women Undergoing Treatment of Index Hip Fractures

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To evaluate the safety and efficacy of AGN1 LOEP to reduce the incidence of secondary hip fractures in subjects presenting with an index hip fracture and undergoing hip fracture repair surgery. AGN1 LOEP treatment outcomes will be compared to a…

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Observational invasive

Summary

ID

NL-OMON54786

Source
ToetsingOnline

Brief title
RESTORE Study

Condition

- Other condition

Synonym
Osteoporosis, porous bone

Health condition

geriatrische aandoeningen en osteoporose (heup)

Research involving
Human

Sponsors and support

Primary sponsor: AgNovos Healthcare USA, LLC
Source(s) of monetary or material Support: Industrie

Intervention

Keyword: AGN1, hip fracture, Local Osteo-Enhancement Procedure, Osteoporosis

Outcome measures

Primary outcome

Primary efficacy endpoint: the cumulative incidence of secondary fragility hip fractures in the contralateral unfractured target hip in the Treated Group compared to the incidence in the Control Group.

Primary safety evaluation: the incidence of all Adverse Events and all Serious Adverse Events in the Treated Group relative to the incidence in the Control Group until the primary efficacy endpoint is reached.

Secondary outcome

1. Total hip areal bone mineral density (aBMD) in target hips of the Treated Group is significantly greater than that of the Control Group at 1 year for all subjects who have achieved 1 year of follow-up by the end of enrollment.

2. Total hip areal bone mineral density (aBMD) in target hips of the Treated Group is significantly greater than that of the Control Group at 2 years for all subjects who have achieved 2 years of follow-up by the end of enrollment.

3. Bone quality as measured by Trabecular Bone Score (TBS) in target hips of the Treated Group is significantly greater than that of the Control Group at 2 years for all subjects who have achieved 2 years of follow-up by the end of

enrollment.

4. Bone quality as measured by Trabecular Bone Score (TBS) in target hips of the Treated Group is significantly greater than that of the Control Group at 1 year for all subjects who have achieved 1 year of follow-up by the end of enrollment.

Study description

Background summary

Fragility fractures of the hip (i.e. a fracture resulting from low-energy trauma, such as a fall from standing height) are associated with significant morbidity and mortality, and represent a significant burden on affected individuals, families, and healthcare systems. Although multiple factors contribute to hip fracture risk, a key factor is osteoporosis, a disease characterized by reduced bone mass, particularly in postmenopausal women who experience more dramatic declines in bone mass than men due to hormonal differences. The loss of trabecular bone caused by osteoporosis is particularly problematic in the hip where a fracture results in the highest morbidity of all fragility fracture locations. The strongest predictors of incident hip fractures seen were prior fracture of the hip. The risk of a secondary hip fracture is highest in the months immediately after the index fracture, a timeframe during which no currently available treatment offers protection. AGN1 LOEP is designed to reduce the risk of secondary contralateral hip fracture by strengthening the proximal femur. After the AGN1 LOEP treatment, the AGN1 implant material provides immediate strength to the proximal femur51. The AGN1 implant material resorbs over time, with greater than 97% resorbed by one year with residual AGN1 incorporated into newly formed trabecular bone. AGN1 implant material resorption is closely coupled to bone formation and as the material resorbs, new bone is formed. This new bone provides long-term strengthening of the proximal femur. The underlying hypothesis is that increasing the strength of the proximal femur will increase the force necessary to fracture the femur from low-energy trauma such as a fall from standing height.

Study objective

To evaluate the safety and efficacy of AGN1 LOEP to reduce the incidence of secondary hip fractures in subjects presenting with an index hip fracture and undergoing hip fracture repair surgery. AGN1 LOEP treatment outcomes will be

compared to a Control Group of subjects not treated with AGN1 LOEP.

Study design

An event driven, randomized, controlled, prospective, single blinded, multi-national study

Study burden and risks

The intended patient population was identified to optimize the benefit/risk profile of the therapy. Intended patients are at high risk for a secondary hip fracture. We estimate that the AGN1 LOEP device effect in reducing the incidence of secondary hip fracture in the intended patient population will be 80%. This estimate is based on correlations between fracture risk and the following parameters: 1) BMD, 2) femoral strength, and 3) bone microarchitecture. Data supporting these correlations are summarized in section 10.1 of the protocol.

There are potential risks associated with study participation, as listed in section 10.2 of the protocol. For subjects assigned to the Control group, risks of participation are negligible since they will receive treatment per standard of care.

Subjects from geriatric (vulnerable) populations are typically at the highest risk of a fragility hip fracture and, therefore, make up a portion of the population that is expected to receive the greatest benefit from the AGN1 LOEP treatment. Thus, inclusion of these subjects is necessary to accurately assess the potential benefit of treatment with AGN1 LOEP.

The burden and risks of study participation is deemed in balance with the expected benefits.

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Elderly (65 years and older)

Inclusion criteria

1. Subject is a postmenopausal female at least 1-year post menses and at least 65 years of age. 2. Subject presents with a low-energy index fragility hip fracture in one hip and will undergo surgical repair of the fractured hip. 3. Subject has at least one of the following additional risk factors for a secondary hip fracture (as determined by subject interview or legally authorized representative (LAR) interview or medical record review): • Documented falls assessment indicating subject is at moderate or high risk of falls • Falls history (2 or more falls in the previous 12 months) • History of vertigo, dizziness, or postural hypotension • Documented T-score < -2.5 at the hip • Taking more than 3 daily prescription medications • Visual impairment as confirmed by one of the following: o Subject reports difficulty seeing o Lack of depth perception or vision loss in one eye o Macular degeneration o Cataracts • Prior non-hip fragility fracture • Cognitive frailty as assessed by SPMSQ (mild cognitive impairment), memory problems, or delirium • Parkinson*s disease stage 3 or 4 • 10-year hip fracture probability >15% using the FRAX® Fracture Risk Assessment Tool of the clinical site country 4. Subject is expected to be ambulatory after the hip fracture repair procedure. 5. Informed consent is provided by the subject or the subject*s LAR 6. The subject*s willingness, ability, and commitment to participate in screening, treatment, and all follow-up evaluations for the full duration of the study has been documented.

Exclusion criteria

1. Subject hospital admission is > 24 hours from the time of the index hip fracture. 2. Subject was dependent on the use of a wheel-chair or was bedridden prior to the index hip fracture. 3. Subject is currently enrolled in another interventional clinical study. 4. Subject has a history of hip surgery or previous hip fracture on the target unfractured hip contralateral to the index hip fracture. 5. Subject has one or more new fractures in addition to the index hip

fracture at admission that, in the opinion of the investigator, would further compromise patient mobility, rehabilitation, and/or recovery or subject has three or more new fractures in addition to the index hip fracture. 6. Subject has an infection at the LOEP intended treatment site or has non-intact skin or acute traumatic injuries with open wounds close to the area of intended LOEP treatment. 7. Subject has a progressive increase in undiagnosed pain in the target hip contralateral to the index fractured hip over the previous 3 months that in the opinion of the Investigator may suggest underlying bone or joint pathology on the unfractured side. 8. Subject has radiological evidence of gross bony or joint pathology of the hip, including signs predictive of atypical femoral fractures (e.g. cortical beaking), or has been diagnosed and/or treated for atypical femoral fractures. 9. Subject is at ASA Class IV, V, or VI. 10. Subject has a history of metabolic bone disease other than osteoporosis (e.g., Paget*s disease, renal osteodystrophy, or osteomalacia). 11. Subject has a history of tuberculous spondylitis. 12. Subject 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. 13. Subject has chronic cardiac insufficiency or severe cardiovascular disease as assessed by a subject or LAR interview to be NYHA Class III or IV or has an implanted pacemaker. 14. Subject has a history of cardiovascular events (e.g. stroke, transient ischemic attack, myocardial infarction, unstable angina, pulmonary embolus, deep vein thrombosis, ventricular tachycardia, or atrial fibrillation) in the last 3 months. 15. Subject is on oral or parenteral immuno-suppressive drugs. 16. Subject has uncontrolled diabetes mellitus. 17. Subject has Hb <= 9 g/dL at admission. 18. Subject has severe renal insufficiency defined as an estimated glomerular filtration rate (eGFR) <= 30 mL/min. 19. Subject has albumin corrected serum calcium levels outside the normal laboratory range or has a pre-existing calcium metabolism disorder (e.g. hypercalcemia). 20. Subject has a Parker Mobility Score <= 5. 21. Subject has moderate or severe cognitive impairment as assessed by an SPMSQ score of 5 or higher. 22. Subject has known allergies to calcium-based bone void fillers. 23. In the judgement of the Investigator, the subject is not a good study candidate (e.g., inability to maintain follow-up schedule, comorbidity or poor general physical/mental health, or drug or alcohol abuse issues). 24. Subject fails pre-operative or intraoperative eligibility criteria Pre-operative eligibility criteria The subject will be evaluated immediately before beginning the hip fracture surgery. The subject will not proceed in the study if they have experienced any of the following changes or complications: • Change in ASA Class to IV, V, or VI • Occurrence or relevant suspicion of cardiovascular events (e.g. stroke, transient ischemic attack, myocardial infarction, unstable angina, pulmonary embolus, deep vein thrombosis, ventricular tachycardia, or atrial fibrillation) • Time from hospital admission to hip fracture repair surgery greater than 72 hours • Any complications or factors that in the judgement of the surgeon or anesthesiologist disqualify the subject from receiving the AGN1 LOEP treatment Intraoperative eligibility criteria Upon completing the hip fracture surgery and before randomization and beginning the AGN1 LOEP treatment, the subject will again be evaluated by the surgeon and anesthesiologist. Intra-operative complications that may result in a Screen Failure and ineligibility for randomization include: • Hip fracture surgery procedure time >120 minutes • Complications during hip fracture repair including but not limited to: o Unstable vital signs (e.g. systolic blood pressure below 80 mmHg that does not respond to treatment, <92% O2 saturation that cannot be corrected) o Intra-operative blood loss >300 ml o Suspected occurrence of bone cement implantation syndrome (BCIS) • Any complications or factors that in the judgement of the surgeon or anesthesiologist disqualify the subject from receiving the AGN1 LOEP treatment

Study design

Design

Study type:	Observational invasive
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Single blinded (masking used)

Primary purpose: Prevention

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-04-2021
Enrollment:	144
Type:	Actual

Medical products/devices used

Generic name:	AGN1 Local Osteo-Enhancement Procedure (LOEP®) Kit
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	21-11-2019
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	03-03-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	21-09-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	31-03-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	29-09-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	02-03-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	24-06-2024
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
ClinicalTrials.gov	NCT04796350

Register	ID
CCMO	NL71436.075.19