A proof-of-concept study of SB-751689 in male and female with a fractured distal radius.

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To evaluate the effects of SB-751689 on the time to radiographic healing, defined as the interval in days between the occurrence of the radial fracture and the time of complete bridging and/or disappearance of fracture line at 3 of the following 4...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Bone disorders (excl congenital and fractures)
Study type	Interventional

Summary

ID

NL-OMON31582

Source
ToetsingOnline

Brief title
SB-751689 in patients with a fractured wrist

Condition

- Bone disorders (excl congenital and fractures)

Synonym
distal radius fracture

Research involving
Human

Sponsors and support

Primary sponsor: GlaxoSmithKline
Source(s) of monetary or material Support: 4e geldstroom (farmaceutische industrie)

Intervention

Keyword: Bone healing, Fracture wrist, Proof of concept, SB-751689

Outcome measures

Primary outcome

Primary objective

To evaluate the effects of SB-751689 on the time to radiographic healing, defined as the interval in days between the occurrence of the radial fracture and the time of complete bridging and/or disappearance of fracture line at 3 of the following 4 cortices: dorsal, volar, radial, or ulnar.

Secondary outcome

Secondary objectives

1. To evaluate the safety and tolerability of SB-751689 administered for a period of 12 weeks compared with placebo

2. To evaluate the dose regimen- and concentration-response relationships for SB-751689 on:

* Serum PTH and calcium concentrations

* Biomarkers of bone turnover: serum cross-linked C-terminal telopeptide 1 chain of type I collagen (CTX), procollagen type 1 N-propeptide (P1NP), bone-specific alkaline phosphatase (BSAP), and osteocalcin (OC) concentrations

3. To evaluate radiographically:

* The baseline incidence of radio-ulnar joint involvement and radiocarpal joint involvement

* The effects of SB-751689 on anatomical deformity of the wrist

4. To evaluate the effects of SB-751689 on the clinical assessment of healing

as defined by presence and/or absence of pain and swelling, and

range-of-motion.

5. To evaluate the effects of SB-751689 on mass grip strength, and to compare

the hand grip strength on both injured and un-injured hands as measured by the

JAMAR hand dynamometer

6. To evaluate the effect of SB-751689 on patient quality of life as assessed

by the Short Form 36 (SF-36)

7. To assess the effect of SB-751689 on patient activities as measured by the

Disabilities of the Arm, Shoulder, and Hand (DASH) questionnaire

Study description

Background summary

SB-751689 is a potent, selective calcium sensing receptor (CaR) antagonist. Blocking calcium receptor activity on the parathyroid gland by SB-751689 will stimulate a transient rise in endogenous parathyroid hormone (PTH) secretion. Fractures are the largest problem facing individuals with bone disease. Wrist fractures are the most commonly occurring fracture in women under the age of 75 in the United States (US) and Northern Europe. The worldwide incidence of wrist fractures is not well known. The estimated lifetime risk of a wrist fracture in women is 16% [Thorpe, 2006]. Currently, no systemic compound is approved for the treatment of fracture healing. The proposed study design focuses on closed fractures of the distal radius. While these fractures are often viewed as simple, the treatment of them has evolved over time and standard of care may vary regionally. The one agreed upon goal of therapy is to restore functional anatomy with restoration of hand function. The demonstrated effects of SB-751689 to release PTH and increase bone formation have led to the proposed hypothesis in this study and may bridge the gap of an unmet need for an effective oral anabolic agent to enhance fracture healing.

Study objective

To evaluate the effects of SB-751689 on the time to radiographic healing, defined as the interval in days between the occurrence of the radial fracture and the time of complete bridging and/or disappearance of fracture line at 3 of

the following 4 cortices: dorsal, volar, radial, or ulnar.

Study design

This is a Phase IIa randomized, double-blind, placebo-controlled, parallel-group, multicenter, proof-of-concept study assessing the efficacy and safety of SB-751689 in accelerating the healing of a closed fracture of the distal radius. Study subjects will be adult men and women.
The study consists of 3 phases: a Screening period of 5 days or less in which subject eligibility is determined (Screening Day -1 to -5), a Treatment Phase of 12 weeks duration in which subjects will make visits to the clinic at Day 0 (Baseline) and Weeks 1, 2, 3, 4, 5, 6, 8, 12, and a Follow-up phase in which subjects will make a single visit to the clinic 4 weeks after the last dose of study medication (Week 16).

Intervention

The doses selected for the study are: SB-751689 at 400 mg once daily, 200 mg twice daily, or placebo for 12 weeks.

Study burden and risks

see answers to questions E7 -E9

Contacts

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Scientific
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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. Informed Consent: Subject is willing and able to provide written informed consent
2. Fracture type: Extra-articular distal radius fractures AO/ASIF types 23-A2 and 23-A3 are permissible.
3. Fracture treatment: Received conservative treatment of the distal radius fracture, including closed reduction and immobilization device
4. Men or Women: Ambulatory males or females aged *35 to < 80 years of age who have sustained a closed, unilateral, fracture of the distal radius no more than 5 days prior to randomization.
5. Protocol compliance

Exclusion criteria

1. Timing of fracture: Any treatment of a fractured distal radius that occurred more than 5 days after the fracture sustaining injury
2. Fracture: All B- and C-type fractures (intra-articular) according to AO Fracture classification that would likely require open reduction and internal fixation
3. Prior fractures: Prior fracture of the same wrist as an adult
6. Bone metabolism: History or concurrent diseases affecting bone metabolism (e.g., osteomalacia, hyperparathyroidism, hyperthyroidism, etc.)
7. Skeleton: History of skeletal immaturity or pathologic (tumor-related) fracture
8. Arthritis
9 Thyroid hormone replacement, Subjects will be excluded if TSH levels are <0.1 or >10.0 mIU/L. If TSH is >4.5 to <10.0 mIU/mL, measure T4 and exclude the subject only if the T4 is outside the normal range
12. Malignancy: Malignant disease diagnosed within the previous 5 years or active peptic ulcer disease
14. Liver disease
15. Drug or alcohol abuse: Drug or alcohol abuse (past or current) within the previous 12 months
18. Surgical and medical conditions

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Double blinded (masking used)
Control:	Placebo
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Will not start
Start date (anticipated):	01-10-2007
Enrollment:	15
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	nog niet toegewezen
Generic name:	ronacaleret

Ethics review

Approved WMO Date:	25-07-2007
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	10-04-2008
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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
Other	clinicaltrials.gov
EudraCT	EUCTR2007-001477-29-NL
CCMO	NL17945.029.07