A 24 weeks multicentre, randomized, double-blind, placebo-controlled, parallel group, study to evaluate the efficacy, safety and tolerability of intravenous IG-8801 20 mg and 40 mg in subjects with chronic low back pain

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To assess, in patients with non-specific low back pain, lasting for over 3 months, the effect of two doses of olpadronate administered intravenously on low back pain as compared to placebo treatment. Assessment of safety and tolerability are also...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON46893

Source
ToetsingOnline

Brief title
Intravenous Olpadronate in chronic low back pain

Condition

- Other condition

Synonym
aspecific low back pain, chronic low back pain

Health condition

degenerative afwijkingen van de lumbale wervelkolom leidend tot axiale aspecifieke en chronische lage rugpijn

Research involving
Human

Sponsors and support

Primary sponsor: Gador S.A.
Source(s) of monetary or material Support: Gador S.A.;Buenos Aires;Argentinië

Intervention

Keyword: chronic, low back pain, non-specific

Outcome measures

Primary outcome

Change from Baseline in pain scores after 24 weeks (part of the Brief Pain

Inventory) measured with an electronic Diary.

Secondary outcome

- The change from baseline in daily average pain intensity score obtained from

electronic diary entries during 7 days prior to the visit at baseline at

visits/call at Week 4, 8 and 12

- The change from baseline in daily worst pain intensity score obtained from

electronic diary entries during 7 days prior to the visit at baseline at time

points Week 4, 8, 12 and 24

- Safety parameters will be obtained via adverse events and laboratory

evaluations. Tolerability will be assessed by infusion site reactions.

- A responder assessment. Response is defined as a decrease from baseline in

the daily average pain score obtained from electronic diary entries during 7

days prior to the visit, by at least 30% or at least 2 points on the BPI pain

scale).

- The use of *rescue medication* will be recorded by the subjects via their

input into their electronic diary.

- Effect of IG-8801 on the outcome of Roland Disability Questionnaire.

- Effect of study treatment on subjects* overall impression of change after

study treatment via Clinical Global Impression rating scale (CGI).

Study description

Background summary

According to the Dutch Standard of Dutch Practitioners, the standard treatment of aspecific chronic low back pain consists of pain killers (simple pain killers and non-steroid ant-inflammatory drugs with analgesic effect), physiotherapy or manual therapy and mental support/coaching. Surgical intervention is not very common.

Standard treatment is effective in a large percentage of patients, however complaints do return within 12 months in 75% of all cases. A small percentage of patients do not benefit or do have too many side effects of the treatment.

Beside their effect on bone metabolism, biphosphonates are known to have an anagesic effect, The mode of action is largely unknown.

A small study published in 2014 with the bisphosphonate pamidronate in subjects suffering from aspecific chronic low back pain demonstrated a clinically significant decrease of pain compared with placebo at the highest dose. Other studies with a more heterogenous study population showed a significant decrease of pain.

Oldapronate is now being tested for the first time in subjects with aspecific chronic low back pain. Aspecific means that there are no speciifc causes for the pain like Paget's disease, ankylsoing spondylitis, bone metastases or neurological disorders like herniation of the intervertebral discs.

"Chronic" implies pain that exists for more than 12 weeks.

Study objective

To assess, in patients with non-specific low back pain, lasting for over 3 months, the effect of two doses of olpadronate administered intravenously on low back pain as compared to placebo treatment. Assessment of safety and tolerability are also objectives of the study.

Study design

This is a multicenter (3), randomised, double blind, placebo controlled study with 3 parallel treatment groups. This is an interventional study.

Intervention

Study subjects will be randomizedin in a 1:1:1 ratio:

- 2 x 10 mg intravenous olpadronate with an interval of 7 days;
- 2 x 20 mg intravenous olpadronate with an interval of 7 days;
- 2 x olpadronate placebo, intravenously,with an interval of 7 days;

Study burden and risks

- 7 visits in 26 weeks
- 2 visits during which a 2-4 hour infusion will be administered with an interval of 7 days. The other 5 visits will have a duration of approximately 1-2 hours
- Risk of "flu-like" symptoms after infusion of the study drug consisting of fever and muscle ache. Paracetamol may be used
- Recording pain score in the electronic Diary
- Several questionnaires
- Sevral times blood sampling
- Several times physical examination
- In the beginning and at the end of the study a MRI of the Lumbar Spine
- In the beginning of the study an X-Ray of the Lumbar Spine.

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

- Informed consent must be given before any assessment is performed
- Men or women of 21 years of age or older
- Axial spine back pain persisting for at least three months
- MRI evidence of disc degeneration and/or any imaging evidence of vertebral changes consistent with the diagnosis of degenerative disc disease, spondylotic disease of the lumbar spine or an old vertebral fracture
- A Baseline Average Pain Intensity of 4 or higher. [subjects will rate their daily average pain intensity, on a scale from 0-10, and enter their response into an electronic diary. Baseline Average Pain Intensity (BSL-API) is calculated from daily average pain intensity scores obtained from electronic diary entries during the 7 days prior to the first infusion at BSL]. Subjects have to fill in the electronic diary correctly 4 days out of 7 as a minimum.
- Subjects who are * in the opinion of the investigator * able to understand all study procedures and willing to comply with all study requirements.

Exclusion criteria

- A history of prior back surgery
- A documented clinical vertebral fracture within 6 months of study entry
- A history of cancer in the past 5 years, except for non-melanoma skin cancer that has been treated with no evidence of recurrence in the past 3 months, carcinoma in situ of the cervix, colon polyps with non-invasive malignancy that have been removed
- A history of hypocalcaemia
- 25-hydroxy Vit D levels < 30 nmol/L (12.5 ng/ml).

- An estimated glomerular filtration rate (GFR) less than 35 ml/min
- Current clinically significant cardiac (e.g. atrial fibrillation), hematological (e.g. anaemia), hepatic (e.g. more than 2 x the upper limit of liver enzymes), endocrine (e.g. primary hyperparathyroidism, uncontrolled hyper- or hypothyroidism), or psychiatric disease (e.g. severe depression)
- Diagnosed metabolic bone disease such as Paget*s disease and Osteogenesis Imperfecta. However, osteoporosis is NOT an exclusion criterion.
- Any prior use of intravenous bisphosphonates or oral bisphosphonates in the last 3 years. Any prior use of any other antiresorptives is NOT an exclusion criterion.
- A known allergy to bisphosphonates
- Pregnant or nursing women, where pregnancy is defined as the state of a female after conception and until the termination of gestation, confirmed by a positive hCG laboratory test (> 5 mIU/mL)
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant, UNLESS they are using a highly effective method of birth control (i.e. one that results in a less than 1% per year failure rate when used consistently and correctly, such as implants, injectables, combined oral contraceptives, and some intrauterine devices (IUDs)). Periodic abstinence (e.g. calendar, ovulation, symptothermal, post-ovulation methods) are not acceptable
- A present history of alcohol abuse
- BDI score of 29 or more
- Subjects have had a tooth extraction or any invasive dental procedure within three months prior to study enrolment; have poor oral hygiene or inadequate dental care in the opinion of the investigator
- Subjects who have received systemic glucocorticoid therapy within 3 months of enrolment in the study;No additional exclusions may be applied by the investigator, in order to ensure that the study population will be representative of all eligible subjects.

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:	Recruitment stopped
Start date (anticipated):	21-06-2016
Enrollment:	57
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	n.v.t.
Generic name:	monosodium olpadronate

Ethics review

Approved WMO Date:	24-02-2016
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	15-03-2017
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	19-02-2018
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	01-03-2018
Application type:	Amendment

Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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
EudraCT	EUCTR2015-004269-96-NL
CCMO	NL55207.098.15

Study results

Date completed:	02-02-2019
Actual enrolment:	58