Study of the analgesic effects of repeated doses of F13640 in spinal cord injury patients with moderate to severe central neuropathic pain.
A multinational, multicenter, randomized, double blind, parallel groups, placebocontrolled study.

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Primary objective:To evaluate the efficacy of F13640 in spinal cord injury patients with moderate to severe central neuropathic pain, when administered for 12 weeks including a 7-day titration period. Main secondary objectives:To evaluate pain...

Ethical review	Approved WMO
Status	Will not start
Health condition type	Spinal cord and nerve root disorders
Study type	Interventional

Summary

ID

NL-OMON31968

Source
ToetsingOnline

Brief title
F13640 GE210

Condition

- Spinal cord and nerve root disorders

Synonym
central neuropathic pain, spinal cord injury

Research involving
Human

Sponsors and support

Primary sponsor: Pierre Fabre
Source(s) of monetary or material Support: Institut de Recherche Pierre Fabre

Intervention

Keyword: analgesic effects, central neuropathic pain, F13640, spinal cord injury

Outcome measures

Primary outcome

The primary criterion is the response to treatment defined as an average decrease from baseline, i.e. the last week before inclusion, of at least 30% on the 24-hour recall pain intensity score recorded on a Numeric Rating Scale by electronic diary within the last week before the end of treatment (D84 or premature withdrawal for any reason other than lack of efficacy); patients in whom the average daily dose of the intake of rescue medication during the last week before the end of treatment has increased by 15% or more compared to the last week before inclusion, will be considered as non responders.

Secondary outcome

Secondary criteria:

- 24-hour recall pain intensity

- Score of pain relief

- Paroxysmal pain

- Brush evoked allodynia test (this test will be done in patients with

allodynia only, on identified allodynia zone, variable according to patients,

but maintained unchanged throughout the study)

- Brief pain inventory (BPI)

- Neuropathic pain symptom inventory (NPSI)

- Sleep Questionnaire (MOS-Sleep Scale)

- Anxiety and depression scale (HADS)

- Quadriceps spasticity and reflexes score (Modified Ashworth scale and Mayo -

Clinic scale)

- Walking scale (WISCI II)

- Spasm scale (Penn)

- Spinal cord independence mesure (SCIM)

- International Index of Erectile Function (IIEF)

- Hoffmann-reflex (H-reflex) of the soleus muscle

- Patient Global Impression of Change (PGIC)

- Amount of rescue medication Safety criteria

Adverse events, vital signs, physical examination, ECG, body weight, laboratory

tests.

PK Blood samples: Four blood samples (out-patient) to six blood samples

(institutionalized patient): one sample on Day 28 and Day 56 and two samples

(with a minimal interval of 2 hours) or four samples on Day 84.

Study description

Background summary

F13640 is a potent and selective 5-HT1A receptor agonist. In pre-clinical studies, F13640 produces powerful analgesia in models of tonic nociceptive pain, chronic nociceptive pain and chronic neuropathic pain of central or peripheral origin. Safety and pharmacokinetic data are available in healthy young male volunteers for single administration up to 2.5 mg and repeated administration up to 2.25 mg/d for 14 days, and in healthy elderly male and female at 1 mg.

Study objective

Primary objective:

To evaluate the efficacy of F13640 in spinal cord injury patients with moderate to severe central neuropathic pain, when administered for 12 weeks including a 7-day titration period.
Main secondary objectives:
To evaluate pain relief, impact on sleep, mood and motricity, safety and tolerability of F13640 in spinal cord injury patients with moderate to severe central neuropathic pain, when administered for 12 weeks including a 7-day titration period.

Study design

Randomized, double blind, parallel groups, placebo-controlled study

Intervention

One group receives tablets of 0.5 mg of F13640 and the other group receives tablets of placebo.
On day 1 and 2, patients will receive 0.5 mg/day of F13640 or placebo. If the patients tolerate this dose, they will be stepped up to a daily dose of 1 mg of F13640 (or placebo) for day 3 and 4, 1.5 mg of F13640 (or placebo) for day 5 and 6 and 2 mg of F13640 (or placebo) from day 7 to day 84.
According to the tolerability evaluations by the investigator from day 4 to day 84, the patient will either be maintained at the same dose or stepped down to the previous level dose. Once the dosage has been maintained or decreased, it should not be increased again.

Study burden and risks

Activity Visit Frequency
Informed Consent V1 1
Selection / Non selection criteria V1 1
Inclusion / Non inclusion criteria V2 1
Randomisation V2 1
Treatment Daily V2-V6 84

Fill-in the PDA Daily 94
Daily telephone contact D2-D6 5
1 telephone contact per week D8-D27 3
Global physical examination V1-V7 7
Vital signs V1-V7 7
ECG V1, V6, V7 3
Demographic data V1 1
Past medical/ surgical history V1 1
Concomitant diseases V1 1
Laboratory tests V1, V2, V4-V7 6
PK samples V4 and V5: 1 sample
V6: 2 or 4 samples 4 of 6
Concomitant treatments V1-V7 7
Questions about adverse events V2-V7, D2-D6, D8-D27 14
DN4 V1 1
ASIA V2 1
24h recall pain Daily in the PDA 94
Paroxysmal pain Daily in the PDA 94
Brush evoked allodynia test V1-V7 7
BPI V2, V4, V6 3
NPSI V2, V4, V6 3
MOS-Sleep V2, V6 2
HADS depression and anxiety V2, V6 2
Hoffmann-reflex V2, V6 2
Mod. Ashworth / Mayo clinic V2, V6 2
WISCI II V2, V6 2
Spams V2, V6 2
SCIM V2, V6 2
IIEF V2, V6 2
PGIC V6 1
See also the flow-chart on the last page of the synopsis on page 21 of the protocol.
Regarding the risks, please see the ICF. The risks are related to the product and to taking the blood samples.

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

- Out patient or institutionalised patient, male or female
- Aged between 18 and 65 years
- Diagnosis of spinal cord injury (post-traumatic, post-ischemic, non progressive myelitis, syringomylia*) for at least 1 year with stable neurological lesions for at least 6 months before the selection
- Diagnosis of central neuropathic pain due to spinal cord injury, based on clinical history, clinical examination and appropriate assessment of patient*s signs and symptoms, according to the International Association for the Study of Pain (IASP) definition
- Pain having persisted continuously for at least 6 months before the selection
- 24-hour recall pain intensity score >= 4 and <= 9 on a 11-point paper numerical rating scale at selection visit
- Record of at least 4 assessable evaluations of the 24-hour recall pain intensity score in the PDA over the 7 days preceding the randomization
- Average 24-hour recall pain intensity score of the last 7 days >= 4 on a 11-point numerical rating scale (NRS on PDA) before randomization visit
- DN4 score >= 4 at selection
- AST/SGOT and ALT/SGPT less than 2 times the upper normal values at the selection
- Creatinine clearance > 60 ml/mn
- QTc less than the upper limit of the normal range at the selection
- For the other laboratory safety tests and ECG parameters, normal or considered as not clinically significant, in the investigator*s opinion
- Patient having given his/her written informed consent or his/her oral informed consent

attested by a witness independent of the investigator and the sponsor, in case of motor function impairement in the arms
- Patients affiliated to a social security system, or is a workers beneficiary (if applicable in the national regulation)
- Patient able to read and understand the text on the PDA screen, able to hear the audible prompts, and able to use a PDA device daily for the whole duration of the study. If the patient is physically unable to use the PDA or to complete self-reporting questionnaires or scales, he/she should be assisted by indentified caregivers.

Exclusion criteria

- All conditions that can interfere with the pain assessment: presence of pain of other origin (nociceptive, inflammatory or peripheral neuropathic pain component) that could confound the assessment of central neuropathic pain related to SCI (for example if the intensity of pain of other origin is higher than the intensity of the neuropathic pain or if the patients are unable to distinguish between neuropathic pain and pain of other origin)
- Demyelinating disease (multiple sclerosis*)
- Complex Regional Pain Syndrome and other above level neuropathic pain
- Pain related to complete cauda equina lesions
- Refractory neuropathic pain (no response to more than 3 therapeutic classes well conducted, previously taken for central neuropathic pain)
- Significant cognitive impairment on the investigator*s opinion
- Severe dysautonomic tension instability
- Hypertension with SBP >160 mm Hg and/or DBP>90 mmHg
- SPB <120 mm Hg in sitting position
- Major depression requiring a pharmacological treatment
- Diabetes mellitus
- Any clinically significant hepatic, renal, respiratory, gastro-intestinal, cardiovascular, autoimmune, hematological, neurological or psychiatric history or current disease unrelated to the cause of neuropathic pain which may interfere with pain evaluation and the course of the study on the investigator*s opinion
- History of alcohol or narcotic abuse within the 6 months preceding the selection or alcohol or narcotic dependence within the 2 years preceding the selection
- Pregnancy or breast-feeding
- Woman of childbearing potential who is unwilling or unable to use a medically accepted and well documented method of contraception (chirurgical or hormonal birth control or intrauterine device only) during 2 months before the inclusion in the study, during the whole duration of the study and up to 1 month after the last dose of the study treatment, in order to avoid pregnancy while being exposed to the study treatment
A pregnancy test will be carried out at the selection visit, on D1 before initiation of the treatment, after the last administration of study treatment on D84 (or PW) and at the end of study visit
Man able to father a child unwilling or unable to practice an effective mean of birth control while participating in this study and up to one month after the last dose of the study treatment

- Intake of any unauthorized treatment which cannot be stopped
- For patients having been treated by a prohibited treatment, a wash-out period of at least 5 T1/2 of the treatment must be respected prior to inclusion on D1
- Patient with previous history of pharmacological sensitivity or hypersensitivity to 5-HT agonists
- History of drug allergy or current allergic reaction
- Patient in the exclusion period of a previous study (at least 5 T1/2 of the previous investigational product)
- Patient involved in any other biomedical research during the study
- Patient who could not be contacted in case of emergency
- Is a family member or work associate (secretary, nurse, technician,*) of the Investigator
- Mentally unable to understand the nature, objectives and possible consequences of the trial; or refusing to subject himself / herself to its constraints
- Has forfeited his/her freedom by administrative or legal award or is under guardianship

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):	01-05-2008
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	F13640

Generic name:	F13640

Ethics review

Approved WMO Date:	03-04-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	16-06-2008
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	09-09-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	12-11-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	18-11-2008
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2007-003230-42-NL
CCMO	NL22233.060.08