An Open-Label Study Investigating Long-Term Safety and Tolerability of Nasalfent (Fentanyl Citrate Nasal Spray) in the Treatment of Breakthrough Cancer Pain (BTCP) in Subjects Taking Regular Opioid Therapy

Published: 21-12-2006
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To investigate the long-term safety, tolerability and acceptability of Nasalfent in the treatment BTCP

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON30752

Source
ToetsingOnline

Brief title
Zie C1a

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
Break ThroughCancer Pain

Research involving
Human

Sponsors and support

Primary sponsor: I3Research
Source(s) of monetary or material Support: Archimedes Development Ltd.

Intervention

Keyword: Breakthrough Cancer Pain, BTCP, Fentanyl Citrate, Nasal Spray

Outcome measures

Primary outcome

Adverse events.

Objective nasal examination.

Subjective nasal assessment.

Withdrawal due to AEs.

Physical examination, including vital signs.

Laboratory assessments.

Subject acceptability assessments.

Secondary outcome

NA

Study description

Background summary

Archimedes Development Ltd. has begun a research study of an investigational drug called Nasalfent as a possible treatment for breakthrough pain in patients with cancer.

Nasalfent is an investigational product not yet approved by the Food and Drug Administration (FDA) in the Unites States or in Europe. The active ingredient found in Nasalfent is called fentanyl. Fentanyl has been approved by governmental agencies (e.g., FDA) in other dosage forms, although not for intranasal (ie, through the nose) delivery.

A previous study has shown that Nasalfent may relieve breakthrough pain in patients with cancer and that pain relief was usually rapid. Previous studies with Nasalfent in normal volunteers and patients with breakthrough cancer pain have shown that the nasal route of delivery is well tolerated.

Study objective

To investigate the long-term safety, tolerability and acceptability of Nasalfent in the treatment BTCP

Study design

This will be an open-label study conducted at multiple centres in the United States, Canada, and Europe. Subjects may be newly enrolled into the study or subjects may enter this study after completing Nasalfent Studies CP043/06/FCNS or CP044/06/FCNS. For newly enrolled subjects, the study consists of 4 phases:·
Screening Phase (up to 10 days).·
Open, Dose-Titration Phase (up to 14 days).·
Open-Label Treatment Phase (up to 16 weeks).·
End-of-Treatment Phase (1 to 14 days after last dose).

For subjects previously enrolled in Study CP043/06/FCNS or CP044/06/FCNS, the study consists of the Open-Label Treatment Phase (up to 16 weeks) and the End-of-Treatment Phase (1 to 14 days after last dose).All subjects will come to the study centre for up to 8 visits. The total duration of individual subject participation is up to approximately 5 months.

Intervention

De veiligheid en bijwerkingen van Nasalfent verder te beoordelen bij gebruik gedurende een langere periode

To evaluate the safety and the side effects of Nasalfent in long term usage

Study burden and risks

The burden and risks associated with participation=
Screeningphase
1-Study doctor or study staff will aks questions about any significant medical conditions that the patient might have, any significant surgical procedures that the patient has undergone, and any medication the patient is taking or have recently taken
2-The weight and height of the patient will be recorded
3-The vital signs (blood pressure and pulse rate) of the patient will be taken. .

4-A physical examination and an examination of the patients nose will be performed.
5-De patient will be asked to complete a questionnaire about his/her pain
6-The blood sample, approximately three (3) teaspoons, will be taken
7-A urine sample will be collected for routine testing.
8-A urine pregnancy test will be performed on all women of childbearing potential
Dose-Titration Phase
1-Study doctor or study staff will aks questions about how the patient feel in general.
2- Study doctor or study staff will aks questions about any medication the patient is taking or have recently taken
3-The patient will be asked to fill out a questionnaire about his/her nose
4-Study doctor or study staff will call the patient daily during the Dose-titration phase to review the use of the medication and help the patient achieve the goal of finding the effective dose of Nasalfent
5-The patient will be asked to use a electronic diary .The electronic diary will be used to collect information each time the patient uses a dose of the study medication

Treatment phase
1-For this visit, the patient will be asked to bring all used and unused study medication canisters as well as the electronic diary to the site.
2-Study doctor or study staff will aks questions about any medication the patient is taking or have recently taken
3-The patient will be given enough medication to last for up to 4 weeks
4-Study doctor or study staff will call the patient every week
5-The patient will be asked to come back after 4 weeks for the next visit
6-The patient will be asked to come back after 8 weeks for the next visit
7-The patient will be asked to come back after 12 weeks for the next visit.during this visit the patients will go through the same activities and treatments as in point 1 to 4.
End of Treatment phase
1-The patient will be asked to come back after 16 weeks for the next visit
2-The patient will be asked to bring all used and unused study bottles and canisters as well as your electronic diary
3-Study doctor or study staff will aks questions about any medication the patient is taking or have recently taken
4-Study doctor or study staff will aks questions about how the patient feel in general.
5-The vital signs (blood pressure and pulse rate) of the patient will be taken. .
6-A physical examination and an examination of the patients nose will be performed.
7-De patient will be asked to complete a questionnaire about his/her pain
8-The blood sample, approximately three (3) teaspoons, will be taken
9-A urine sample will be collected for routine testing.

10-A urine pregnancy test will be performed on all women of childbearing potential

The risks and side effects of the study medication associated with participation=side effects of the study medication (See patient information sheet)

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

Subjects will be included in the study if they meet all of the following criteria:
1. Subjects who are able and willing to provide written informed consent.
2. Male or female subjects, 18 years of age and older.

3. If female, and of childbearing potential (not surgically sterile or <=1 year after the onset of amenorrhea due to menopause), must (a) have a negative serum pregnancy test, (b) not be lactating, and (c) agree to practice a reliable form of contraception or abstinence during the study.
4. Subjects who have a histologically documented diagnosis of a malignant solid tumor or a hematological malignancy causing cancer-related pain.
5. Subjects who are taking at least 60 mg oral morphine or equivalent for at least 1 week for cancer-related pain as regular, 24-hour medication for their underlying persistent cancer pain.
6. Subjects who are experiencing, on average, but not necessarily every day, 1 to 4 episodes of BTCP per day that are adequately controlled with a stable dose of standard rescue medication, typically a fast-acting opioid, of which the subject should have an adequate supply throughout the study. Breakthrough pain is defined as a transitory flare of moderate to severe pain (on a 4 point scale from 0 to 3; none, mild, moderate, severe) that occurs on a background of persistent pain controlled to moderate intensity or less (as defined by the Breakthrough Pain Questionnaire) by the opioid regimen. If the subject has more than 1 type of breakthrough pain, or has breakthrough pain in more than 1 location, only 1 of the pains will be identified as a *target* breakthrough pain.
7. Subjects who, in the opinion of the investigator, are willing and able (personally or with the help of a caregiver) to
a. Evaluate and record pain intensity and pain relief.
b. Assess medication performance at specific times after dosing.
c. Record adverse events.
d. Record each instance of the use of study drug, standard rescue medication, and other medications in a subject diary for the duration of the study.
8. Subjects with an Eastern Cooperative Oncology Group (ECOG) score of <=2 and a life expectancy which, in the opinion of the investigator, will allow them to participate for the duration of the study.

Exclusion criteria

Subjects may be excluded from participating in the study if they meet any of the following criteria:
1. Subjects with an opioid or fentanyl intolerance.
2. Subjects with uncontrolled or rapidly escalating pain.
3. Subjects using intrathecal or epidural opioids.
4. Subjects whose condition is unstable or rapidly deteriorating that the effective dose found during the Open, Dose-Titration Phase is unlikely to remain so for the duration of the study.
5. Subjects with sleep apnea or active brain metastases with increased intracranial pressures.
6. Subjects with any respiratory or cardiac condition that, in the opinion of the investigator, may be worsened by opioids.
7. Subjects with any other medical condition that, in the judgment of the investigator, would confound the objectives of the study.
8. Subjects with a recent history of alcohol or substance abuse that would compromise data collection.

9. Subjects with a history of or current neurological or psychiatric impairment, or cognitive dysfunction that, in the opinion of the investigator, would compromise data collection.
10. Subjects with clinically significant renal and hepatic dysfunction test results at Screening outside the following limits:
a. Serum creatinine must be <=2.0 mg/dL, or creatinine clearance calculated by Cockcroft-Gault formula must be >=50 mL/min.
b. Serum total bilirubin must be <=2.0 mg/dL.
c. Serum aspartate aminotransferase (AST), alanine aminotransferase (ALT), and alkaline phosphatase must be <=3 times the upper limit of normal (<=5 times the upper limit of normal if due to liver metastases).
11. Subjects taking any medication likely to affect the physiology of the nasal mucosa.
12. Any abnormal nasal physiology and/or pathology which, in the opinion of the investigator, would not allow the objectives of the study to be accomplished.
13. Subjects with known intolerance to nasal sprays and/or pharmaceutical materials found in the investigational products.
14. Subjects taking monoamine oxidase inhibitors (MAOIs) within 14 days of the screening visit or with an anticipated need for MAOIs during the study.
15. Subjects taking analgesics (other than that taken for underlying persistent cancer pain) for less than 21 days prior to the screening visit, even at a stable dose.
16. Subjects receiving antiepileptics for neuropathic pain (such as gabapentin, topiramate, lamotrigine) that is not the target breakthrough pain for less than 14 days prior to screening.
17. Subjects with uncontrolled infection.
18. Subjects who have received treatment with an investigational drug within 4 weeks of the screening visit.
19. Subjects who have had treatment with any form of radiotherapy within 30 days prior to study entry or who have had any therapy that could alter pain or response to pain medication.
20. Subjects planning to undergo chemotherapy (unless it has been demonstrated in that subject to have no effect on the breakthrough cancer pain), radiotherapy, or surgery during the treatment period.
21. Subjects whose primary source of breakthrough pain is not cancer related.

Study design

Design

Study phase:	3
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	13-12-2006
Enrollment:	36
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Fentanyl Citrate Nasal Spray
Generic name:	Nasalfent

Ethics review

Approved WMO Date:	21-12-2006
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	14-06-2007
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-08-2007
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	22-01-2008
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	24-07-2008
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO	

Date:	24-09-2008
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	27-01-2009
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	20-05-2009
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	30-11-2009
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

No registrations found.

In other registers

Register	ID
EudraCT	EUCTR2006-0054-03-3-NL
CCMO	NL15359.028.06