A Randomized, Double-Blind, Placebo-Controlled, Multicenter Study to Evaluate the Efficacy, Safety, and Tolerability of JNJ-42160443 as Adjunctive Therapy in Subjects With Cancer-Related Pain, Followed by an Open-Label Extension Phase

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Ethical review	Approved WMO
Status	Will not start
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON34218

Source
ToetsingOnline

Brief title
Efficacy of JNJ-42160443 in Cancer-Related Pain.

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
cancer-related pain, oncological pain

Research involving
Human

Sponsors and support

Primary sponsor: Janssen-Cilag
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: cancer -related pain, double- blind, multicenter, placebo-controled

Outcome measures

Primary outcome

The primary efficacy evaluation is the average cancer-related pain intensity in the last 24 hours recorded daily on the diary during the double-blind treatment phase using an 11-point NRS, with 0=no pain and 10=pain as bad as you can imagine. The primary efficacy endpoint is the change from baseline to the end of the double-blind treatment phase in the average cancer-related pain intensity score, averaged over the last 3 days before randomization and over the last 7 days of the double-blind treatment phase. The average cancer-related pain intensity score is based on the average pain in the last 24 hours item recorded daily in the diary.

The primary objective of this study is to evaluate the analgesic efficacy, safety, and tolerability of a single SC dose (9 mg in 0.9 mL) of JNJ-42160443 compared with placebo as adjunctive therapy to standard pain therapy in subjects with inadequately controlled, moderate to severe, chronic, cancer-related pain. The primary efficacy objective of this study is also to evaluate the analgesic effect of JNJ-42160443 compared with placebo, as

measured by the change from baseline to the end of the double-blind treatment phase in the average cancer-related pain intensity score, using an 11-point numerical rating scale (NRS), with 0=no pain and 10=pain as bad as you can imagine.

Secondary outcome

The secondary objectives of this study are to evaluate the efficacy of JNJ-42160443 compared with placebo, as measured by the Brief Pain Inventory (BPI) Short Form, Patient Global Impression of Change (PGIC), and baseline and breakthrough opioid use and to evaluate the immunogenicity (antibodies to JNJ-42160443) associated with JNJ-42160443 treatment. The pharmacokinetics of JNJ-42160443 after SC doses will also be examined. The exploratory objectives of this study are to investigate the effects of improvements in pain relief with JNJ-42160443 on the severity of fatigue, aspects of daily activities, and anxiety/depression.

Study description

Background summary

Antibodies are proteins produced naturally by your body are produced and involved in numerous mechanisms such as infection control or vreemde protein destruction. JNJ-42160443 is an artificial antibody specific technologies will be created. JNJ-42160443 binds to a protein in your blood , which thus made inactive, namely nerve growth factor (NGF). Studies in animals and humans have shown that an excess amount of the nerve growth factor in the blood responsible for the pain. Moreover, studies in animals and humans with other experimental treatments were used, the amount of nerve growth factor in the blood were reduced, thereby demonstrated that the pain decreased. This does not mean that JNJ-42160443 will be effective in your case.

Study objective

The objective of this study is to evaluate the safe use of JNJ-42160443 compared to placebo and to demonstrate whether patients JNJ-42160443 will, in addition to their standard treatment for pain, more pain relief than more patients receiving placebo and standard treatment for pain will . The placebo looks just like the product JNJ-42160443 and is administered by the same procedure, but contains no active ingredient. Patients receive an injection every four weeks, for JNJ-42160443 has a long duration. One of the other objectives of this study is to evaluate the effects of JNJ-42160443 compared to placebo on the use of opioids as pain therapy (based treatments and treatments for acute pain).

Study design

Approximately 90 subjects are randomly assigned to treatment, with two thirds of the subjects treated with JNJ-42160443, and about one third treated with placebo. The study consists of a screening phase lasting about 14 days, followed by a double-blind treatment phase lasting about 4 weeks. Subjects double-blind treatment phase completion are eligible for the open-label extension phase based on the discretion of the investigator and maintaining the security of the subject. The duration of the open-label extension phase to a maximum of 56 weeks (including treatment to week 48 and post-treatment phase [final follow-up] to 12 weeks after the last administration of study drug) for each subject. Subjects double-blind treatment phase completion or to evade withdraw and not continue in the open-label extension phase, given a treatment phase (final follow-up) for 8 additional weeks (12 weeks after administration of study drug) for subjects who do not go into the open label extension phase.

Intervention

Approximately 90 subjects are randomly assigned to treatment, with two thirds of the subjects treated with JNJ-42160443, and about one third treated with placebo, this product is a once every 4 weeks subcutaneously.

Study burden and risks

It is possible that there are problems and side effects of treatment intervention studies that are currently not known, these effects could include a worsening of pain or side effects. (This is named in the investigator brochure of this product).

The drawing of the blood can hurt at the puncture site. The penetration may also cause some irritation. Sometimes it creates a (small), bruise or an infection at the puncture site. In some cases, people fainting during blood collection.

There is a possibility of local skin irritation and / or itching occur by the

electrodes on the skin, for the recording of an electrocardiogram (ECG).

Contacts

Public
Janssen-Cilag

dr Paul Janssenweg 150
5000 LT Tilburg
Nederland
Scientific
Janssen-Cilag

dr Paul Janssenweg 150
5000 LT Tilburg
Nederland

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

• Have a life expectancy of at least 3 months • Have a diagnosis of moderate to severe pain directly related to an active form of cancer and inadequately controlled by standard pain therapies; the primary site of pain should not be pain due to treatment of the cancer (eg, post-operative or procedural pain, chemotherapy- or radiotherapy-induced pain, or pain due to other comorbidities related to the cancer (eg, chronic postherpetic neuralgia, chemotherapy-induced neuropathy, osteoporotic fractures) • Currently receiving opioid analgesics at screening: - The baseline, around-the-clock dose should be >=60 mg of oral morphine equivalents, not including breakthrough pain medication doses - The baseline opioid dose should be given as a sustained-release formulation at a stable dose for at least 1

week before screening - A stable, baseline opioid dose is defined as a dose that does not fluctuate by more than 50% from the average dose over the 1 week before screening; the dose may fluctuate by more than 50% for up to 2 days, if medically necessary - The baseline opioid dose is expected to remain stable during the double-blind treatment phase - Not more than an average of 4 breakthrough pain medication doses per day during the 1 week before screening • If currently receiving nonopioid analgesics and adjuvant pain therapies (eg, anticonvulsants, antidepressants, NSAIDs, corticosteroids, pharmaceutical cannabinoids [eg, Marinol®, Sativex®, Cesamet*]), must be at stable doses for at least 1 week before screening and expected to remain stable during the double-blind treatment phase • Have an average daily pain intensity score of >=4 averaged over the last 3 days before randomization (Day 1), where the minimum single assessment score is >=2, and a worst pain score of >=5 averaged over the last 3 days before randomization, using an 11-point NRS, with 0=no pain and 10=pain as bad as you can imagine. Subjects must have recorded NRS pain assessments in their diary for at least 2 of the 3 days before randomization to determine eligibility for entry into the double-blind treatment phase. To be eligible to enter the open-label extension phase, the following key criterion must be met: -Must have completed the double-blind treatment phase of the study -Women of childbearing potential must have a negative urine B-hCG pregnancy test at the end of the double-blind treatment phase (Day 29) -Subjects can participate in 2 trials simultaneously during the open-label extension phase if the other investigational drug is approved in the local country and the side effect profile is well documented. Each case must be pre-approved by the J&J PRD medical monitor. Breakthrough pain medication trials will be handled on a case by case basis.

Exclusion criteria

• Presence of neurologic deficits that are: - Grade 3 or higher motor or sensory deficits, graded according to the Modified Neuropathy Common Terminology Criteria for Adverse Events, or - Unstable or progressive, or - Stable for <3 months before screening, or - Caused by a potentially progressive disease process (eg, hereditary sensory motor neuropathy or other inherited or acquired muscular disease), with the exception of diabetic peripheral neuropathy • Bradycardia (ie, heart rate <60 bpm), or heart rate <50 bpm if the subject is taking heart rate lowering medication (eg, beta blockers) • Significant orthostatic hypotension as defined by: - Symptomatic (ie, feeling dizzy, light headed, or fainting) accompanied by either a decrease in systolic blood pressure of >20 mm Hg or decrease in diastolic blood pressure of >10 mm Hg within 3 minutes of standing up, or - a decrease in systolic blood pressure of at least 40 mm Hg within 3 minutes of standing up, or - a decrease in diastolic blood pressure of at least 20 mm Hg within 3 minutes of standing up • History of bone marrow transplant (BMT) within the past 10 years. If a subject had BMT >10 years ago, must not have had a history of graft versus host disease and not currently receiving immunosuppressive therapy. • History of leukemia • History of small cell lung cancer • History of neuroendocrine tumors • History of any of the following: - Seizure disorders within the past year - Multiple sclerosis within the past year - Intrathecal therapy, Ommaya reservoirs, and ventricular shunts within the past year - Radiotherapy to the cerebral or spinal areas within 3 months before the screening visit - Mild or moderate traumatic brain injury within the past year - Stroke within the past year - Transient ischemic attack within the

past year - Severe traumatic brain injury within the past 15 years (consisting of >= 1 of the following: brain contusion, intracranial hematoma, either unconsciousness or posttraumatic amnesia lasting more than 24 hours) or with residual sequelae suggesting transient changes in consciousness - Any other condition suggesting compromised blood brain barrier (contact the sponsor*s medical officer to discuss if unclear) • Presence of known or suspected cerebral metastases • Any other condition suggesting compromised blood brain barrier (contact the sponsor*s medical officer to discuss if unclear) • Presence of disseminated or severe organ-related herpes virus disease (eg, cytomegalovirus retinitis or cytomegalovirus nephritis) • Presence of severe chronic obstructive pulmonary disease (COPD) • Oxygen saturation (SpO2) <90% on room air or <=2 L/min of oxygen therapy for subjects who have clinically significant compromised lung function. Subjects who are receiving >2 L/min of oxygen therapy will also be excluded irrespective of their oxygen saturation value at screening. • Alanine aminotransaminase (ALT) or aspartate aminotransaminase (AST) >=3 times the upper limit of normal (ULN) • Serum creatinine of >=2 mg/dL • Planned initiation of new chemotherapy regimen or radiotherapy, bisphosphonates, or hormonal or growth factor therapy during the double-blind treatment phase • Planned major surgical procedure during the double-blind treatment phase • Currently using patient-controlled analgesia or IV opioids as chronic baseline pain therapy • Currently receiving >=60 mg-equivalents of prednisone per day • Received an investigational drug (including vaccines) or used an investigational medical device within 30 days before the planned start of treatment, enrolled in an investigational study for an analgesic within the previous 4 weeks or 5 half-lives of the investigational drug (whichever is longer), or are currently enrolled in another investigational study at the time of screening.

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
Enrollment:	32

Type:	Anticipated

Ethics review

Approved WMO Date:	26-07-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)
Approved WMO Date:	06-12-2010
Application type:	First submission
Review commission:	METC Leids Universitair Medisch Centrum (Leiden)

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	EUCTR2008-007690-21-NL
CCMO	NL32989.058.10