An International, Randomized, Double-Blinded, Phase 3 Efficacy Study of XL184 versus Placebo in Subjects with Unresectable, Locally Advanced, or Metastatic Medullary Thyroid Cancer

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To evaluate PFS with XL184 treatment as compared with placebo in subjects with unresectable, locally advanced, or metastatic MTC to see if the investigational drug XL184 is effective in delaying the growth of the tumor.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Endocrine neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON35202

Source
ToetsingOnline

Brief title
Exelixis MTC - XL184-301

Condition

- Endocrine neoplasms malignant and unspecified

Synonym
locally advanced, or metastatic medullary thyroid cancer, unresectable

Research involving
Human

Sponsors and support

Primary sponsor: Exelixis, Inc.
Source(s) of monetary or material Support: Farmaceutische Industrie

Intervention

Keyword: Medullary thyroid carcinoma (MTC)

Outcome measures

Primary outcome

The primary efficacy analysis in this study is the comparison of

progression-free survival (PFS) in subjects treated with XL184 versus placebo.

For the primary endpoint, PFS is defined as time from randomization to PD per

mRECIST as determined by a independent committee or death from any cause if

earlier.

Secondary outcome

The two key secondary endpoints are: Objective Response Rate (ORR) and Overall

Survival (OS).

Study description

Background summary

Thyroid cancer is the most common endocrine malignancy. Medullary Thyroid Cancer (MTC) is an aggressive form of thyroid cancer with 10-year survival rates of 40-50 % for subjects wit metastatic disease. Currently available therapies for MTC are not curative and no large scale or phase-3 study has been conducted. There is a clear need for novel therapeutics in the treatment of MTC. XL184 is a new chemical entity that inhibits growth and angiogenic aspects of the tumor.

Study objective

To evaluate PFS with XL184 treatment as compared with placebo in subjects with

unresectable, locally advanced, or metastatic MTC to see if the investigational drug XL184 is effective in delaying the growth of the tumor.

Study design

The study consists of 3 periods:
1) Screening - screening procedures will be performed within a period of 28 days
2) Treatment - Patients will receive a daily dose of 175mg XL184 in 4-week cycli. During the first 2 cycles, the patient will visit the hospital 5 times for evaluation and every 4 weeks starting with cycle 3. A tumor assessment will be performed once every 12 weeks. Treatment will continue until disease progression.
3) Post- Treatment - Patient will return to the study site 30 days after the last dose of study treatment. Follow-up information will be obtained every 12 weeks.

Intervention

Study treatment will be administered orally at a dose of 175 mg XL184 or placebo once daily in 4-week cycles. Hematology and serum chemistry laboratory evaluations and assessments of vital signs will be conducted every 2 weeks during Cycles 1 and 2, and every 4 weeks starting with Cycle 3.Tumor assessments will be performed every 12 weeks from randomization until PD as determined by the investigator per mRECIST

Study burden and risks

Side effects reported related to treatment with XL184 and experienced by at least:

* 20% of the subjects: Fatigue, diarrhea, loss of appetite, nausea, constipation, vomiting, elevated blood pressure, hoarseness of the voice, blisters, rash or pain in hands or feet.
* 5-20% of the subjects: changes in liver function which may indicate liver damage, headache, shortness of breath, weight loss, abdominal pain, changes to the way things taste or dry mouth, mouth sores / swelling or pain, increased amylase or lipase values, dry skin, infection, back pain, heartburt, loss of hair color or skin color, dizziness, insomnia, confusion, swelling of the hands / legs / feet, dehydration, increased levels of protein in the urine, seizure, decreased amounts of potassium / magnesium / phosphorus / platelet counts / sodium, urinary tract infection, depression, difficulty remembering things, anxiety, blood clots, anemia, joint or muscle pain, bloody nose, increase levels of glucose, difficulty swallowing, difficulty walking normally, fever, flatulence, upper respiratory tract infection, hemorrhoids, muscle spams, itchy skin.

Contacts

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Exelixis, Inc.

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Exelixis, Inc.

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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. The subject has a histologically confirmed diagnosis of MTC that is unresectable, locally advanced, or metastatic, and disease that is measurable or non-measurable per mRECIST.
2. The subject is at least 18 years old.
3. The subject has an ECOG (Eastern Cooperative Oncology Group) performance status <= 2.
4. The subject has documented progressive disease (PD) on computerized tomography (CT), magnetic resonance imaging (MRI) bone scan, or X-ray (determined by the investigator) per mRECIST at screening compared with a previous image done within 14 months of screening.
5. The subject has recovered to National Cancer Institute (NCI) Common Terminology Criteria for Adverse Events (CTCAE) v3.0 Grade <= 1 from clinically significant adverse events (AEs) due to antineoplastic agents, investigational drugs, or other medications that were administered prior to randomization.
6. The subject has organ and marrow function as follows: absolute neutrophil count >=

1500/mm3, platelets >= 100,000/mm3, hemoglobin >= 9 g/dL, bilirubin <= 1.5 times the upper limit of normal (does not apply to subjects with Gilbert*s syndrome), serum creatinine <= 1.5 mg/dL, and alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <= 2.5 times the upper limit of normal.

Exclusion criteria

1. The subject has received prior systemic anti-tumor therapy (eg, chemotherapy, biologic modifiers, or anti-angiogenic therapy) within 4 weeks of randomization (6 weeks for nitrosoureas or mitomycin C).
2. The subject has received radiation to >= 25 % of bone marrow.
3. The subject has received treatment with other investigational agents within 4 weeks of randomization.
4. The subject has received treatment with XL184.
5. The subject has brain metastases or spinal cord compression, unless completed radiation therapy >= 4 weeks prior to randomization and stable without steroid and without anti-convulsant treatment for >= 10 days.
6. The subject has a history of clinically significant hematemesis or a recent history of hemoptysis of > 2.5 mL of red blood or other signs indicative of pulmonary hemorrhage or evidence of endobronchial lesion(s).
7. The subject has a urine protein/creatinine ratio of >= 1 (reported in grams of protein over grams of creatinine).
8. The subject has serious intercurrent illness, such as hypertension (two or more blood pressure readings performed at screening of > 140 mmHg systolic or > 90 mmHg diastolic) despite optimal treatment, unhealed wounds from recent surgery, or cardiac arrhythmias; or a recent history of serious disease such as either symptomatic congestive heart failure or unstable angina pectoris within the past 3 months, or myocardial infarction, stroke, or transient ischemic attack within the past 6 months.

Study design

Design

Study phase:	3
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):	06-07-2009
Enrollment:	13
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	-
Generic name:	cyclopropane-1,1-dicarboxylic acid [4-(6,7-dimethoxy-quinolin-4-yloxy)-phenyl]-amide(4-fluoro-phenyl

Ethics review

Approved WMO Date:	14-11-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	05-02-2009
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	16-09-2009
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	09-02-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	12-04-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Approved WMO Date:	26-11-2010
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	19-04-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	20-10-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	04-11-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	13-12-2011
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	EUCTR2008-002320-29-NL

Register	ID
ClinicalTrials.gov	NCT00704730
CCMO	NL25520.042.08