A Randomized, Double-blind, Placebo-controlled, Phase 3 Study of OSI-906 in Patients with Locally Advanced or Metastatic Adrenocortical Carcinoma

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The primary objective of this study is to determine the overall survival (OS) of single agent OSI-906 (Arm A) versus placebo (Arm B) in patients with adrenocortical carcinoma (ACC) who received at least 1 but no more than 2 prior drug regimens.

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

Summary

ID

NL-OMON36718

Source
ToetsingOnline

Brief title
OSI-906-301

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
adrenocortico carcinoma, kidney cancer

Research involving
Human

Sponsors and support

Primary sponsor: Astellas Pharma

Source(s) of monetary or material Support: OSI pharmaceuticals

Intervention

Keyword: Adrenocortical carcinoma, locally advanced/metastatic

Outcome measures

Primary outcome

To determine the overal survival of OSI-906 (arm A) versus placebo (arm b) in

patients with adrenocortical carcinoma who received at least 1 but no more than

2 prior drug regimens.

Secondary outcome

• progression-free survival, disease control rate, best overall response rate,

and duration of response;

• quality of life

• the safety profile of OSI-906;

• the pharmacokinetic profile of OSI-906; and

• pharmacodynamic changes and correlations with treatment outcome.

Study description

Background summary

ACC is a very aggressive tumor without effective therapy options. Median survival in metastasized disease is less than 15 months. Thus far, mitotane is the only therapy approved for treatment of ACC and there is currently no standard of care for second- or third-line treatment of locally advanced/metastatic disease. OSI-906 is a small molecule that is a potent inhibitor of IGF-1R tyrosine kinase activity. The overexpression of IGF-2 that is frequently observed in ACC could lead to activation of both IGF-1R and the insulin receptor A (IR-A) isoform. OSI-906 has inhibitory activity against both IGF-1R and IR-A. OSI-906 might therefore be expected to have more activity in

ACC.

Study objective

The primary objective of this study is to determine the overall survival (OS) of single agent OSI-906 (Arm A) versus placebo (Arm B) in patients with adrenocortical carcinoma (ACC) who received at least 1 but no more than 2 prior drug regimens.

Study design

Approximately 135 adult patients worldwide will be randomized in 45 centers. This is a multicenter, randomized, double-blind, placebo-controlled, phase 3 study. The study exist of a screening visit and a treatment period. If the patient is eligible, the patient has to visit the clinic once every 3 weeks as long as the patients receives OSI-906/placebo. Every visit takes approximately 4 hours. The patient will be asked on day 1 and day 22 to stay at the clinic for a time period of 8 hours. During the first 3 weeks the patient has to visit the clinic or another location once a week for blood examination. The treatment period is 21 days. When the patient is still in study after 6 months, the treatment period will become 42 days.

Intervention

Blood draws, urine collection and if needed a biopsy.

Study burden and risks

OSI-906 can, besides the possible effect on cancer cells, also have an effect on several organs or others parts of the body.

Based on early results from human studies, the following events are now considered to be related to OSI-906:
• Elevated blood sugar (glucose)
• Nausea
• Vomiting
• Tiredness or fatigue
• Rash
• Itchiness
• Diarrhoea

In non-human studies, an effect of OSI-906 included:
• May effect the electrical activity of the heart which rarely may lead to a serious abnormality of your heart rhythm.

As with any drug, an allergic reaction is possible; some allergic reactions can

be life-threatening. There may also be side effects that we don*t know about yet.

Other potential risks include:
The most common side effects associated with taking blood samples from the arm through a vein may include discomfort or pain where the needle is introduced, redness, bruising, light-headedness, bleeding at the puncture site and on rare occasions infections.

Fasting (not eating or drinking for several hours) before blood draws can cause dizziness, headaches, stomach discomfort or fainting.

Dexamethasone (a steroid) may be given as a single dose for the dexamethasone suppression test. A single moderate dose of oral dexamethasone is not expected to have any significant side effects except possibly some nausea. Severe allergic reactions are rare. However, long term use of dexamethasone is associated with many significant side effects. You should discuss any concerns with your study doctor.

PREGNANCY / CONTRACEPTION
The effect that OSI-906 may have on an unborn or nursing baby is not known. Pregnant women must not take part in this study; neither should women who plan to become pregnant or who are breast-feeding a baby. Women who can have children will be asked to have a pregnancy test before taking part to exclude the possibility of pregnancy. Both women and men (and their partners), who are sexually active and possibly fertile, will be asked to use an effective means of birth control while taking part in this study.

Contacts

Public
Astellas Pharma

3 Parkway North
60015, Deerfield, IL
US
Scientific
Astellas Pharma

3 Parkway North
60015, Deerfield, IL
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- Histologically confirmed adrenocortical carcinoma that is locally advanced or metastatic and not amenable to surgical resection.
- Measurable disease according to RECIST (version 1.1).
- Radiologically-confirmed progressive disease within 6 months prior to randomization.
- Age >= 18 years .
- Predicted life expectancy >= 12 weeks.
- At least 1 but no more than 2 prior drug regimens (including molecular targeted therapy, systemic cytotoxic chemotherapy, biologics, and/or vaccines) for locally advanced/metastatic ACC. A minimum of 3 weeks must have elapsed between the end of prior treatment and randomization. All patients must have received prior mitotane, either as neoadjuvant, adjuvant, or locally advanced/metastatic therapy. Adjuvant and neoadjuvant mitotane therapy will not be counted as prior drug regimens or as systemic cytotoxic chemotherapy.

Exclusion criteria

- Type 1 diabetes mellitus or Type 2 diabetes mellitus currently requiring insulinotropic or insulin therapy.
- Prior IGF-1R inhibitor therapy.
- History of prior malignancy, except for resected basal cell or squamous cell carcinoma of the skin, cured in situ cervical carcinoma, cured ductal carcinoma in situ of the breast, or other cancers where the patient has been disease-free for >= 3 years.
- History of significant cardiovascular disease unless the disease is well-controlled.
- History of cerebrovascular accident (CVA) within 6 months prior to randomization or that resulted in ongoing neurologic instability.

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):	18-01-2010
Enrollment:	20
Type:	Actual

Medical products/devices used

Product type:	Medicine

Ethics review

Approved WMO Date:	09-10-2009
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	22-12-2009
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	03-03-2010
Application type:	Amendment

Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	22-03-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	01-04-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	26-04-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	01-06-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	07-07-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	21-09-2010
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	14-02-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	05-04-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	26-04-2011
Application type:	Amendment

Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	20-05-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	11-08-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	25-08-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	07-10-2011
Application type:	Amendment
Review commission:	METC Maxima Medisch Centrum (Veldhoven)

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	EUCTR2009-012820-97-NL
ClinicalTrials.gov	NCT00924989
CCMO	NL29658.015.09