Efficacy of adjuvant mitotane treatment in prolonging recurrence -free survival in -patients with adrenocortical carcinoma at low-intermediate risk of recurrence

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Primary objectiveTo compare the efficacy of adjuvant mitotane treatment vs observational follow-up only in prolonging recurrence free survival (RFS) in patients with ACC after complete resection and low-intermediate risk for disease recurrence....

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Adrenal gland disorders
Study type	Interventional

Summary

ID

NL-OMON36658

Source
ToetsingOnline

Brief title
ADIUVO

Condition

- Adrenal gland disorders

Synonym
adrenocortical carcinoma, carcinoma of the adrenal cortex

Research involving
Human

Sponsors and support

Primary sponsor: Azienda Ospedaliera S. Luigi Gonzaga

Source(s) of monetary or material Support: HRA Pharma,medicatie en analysering van circulerende mitotane spiegels worden door bedrijf gesponsord;de rest uit eigen middelen onderzoekers

Intervention

Keyword: adrenocortical carcinoma, mitotane

Outcome measures

Primary outcome

Recurence free survival, defined as the time between the date of randomization

until documentation of any of the following failures (whichever occurs first):

- local or distant recurrence of ACC

- death from any cause or completion of follow-up

Secondary outcome

- Overall survival, defined as the time between the date of randomization and

the date of of death from any cause

- Time to recurrence, defined as the time between the date of randomization

until documentation of local or distant recurrence of ACC, or death from ACC

- disease free survival, defined as the time between the date of randomization

until documentation of any relevant cancer disease, or death of any cause

(whichever occurs first)

- Quality of life measured by EORTC-QLQ-C30

Study description

Background summary

Adrenocortical carcinoma is a very rare disease with a high risk of relapse
after radical surgery. The efficacy of adjuvant mitotane treatment is suggested

by a retrospective multicenter international study showing that postoperative mitotane treatment was associated with a significant reduction of the risk of relapse and death. However, these promising results need confirmation in a randomized prospective study. Caution should be adopted particularly in patients with low risk of disease relapse, in whom the benefit of therapy should be weighted agaisnt the side effects. Even if an adjuvant treatment seems justified in patients at high risk of relapse, a randomized prospective study is needed to assess whether such a treatment is efficacious in patients at low-intermediate risk.

Study objective

Primary objective
To compare the efficacy of adjuvant mitotane treatment vs observational follow-up only in prolonging recurrence free survival (RFS) in patients with ACC after complete resection and low-intermediate risk for disease recurrence.

Secondary objectives
* Comparison of Overall Survival (OS)
* Comparison of time to recurrence (TTR)
* Comparison of disease free survival (DFS)
* Quality of life assessment
* Assessment of toxicity
* Assessment of the impact of mitotane plasma levels and time needed to reach the therapeutic interval on the efficacy of treatment
* Assessment of the efficacy of the mitotane administration in predefined subgroups of patients stratified according to:
- type of hormone secretion,
- stage of disease,
- histopathologic characteristics .

Study design

Prospective ,randomized , controlled, open-label, multi-center phase lll trial

Intervention

Patients will be randomly assigned to receive mitotane treatment or observational follow up only. The daily dose of the drug should be increased if plasma levels of the mitotane are below 14 mg/l. Reduction of mitotane dosage should be considered if plasma levels are over 20 mg/l or toxicity does occur. Mitotane will be administered until progression or unacceptable toxicity for a minimum of 2 years.

Study burden and risks

The burden and risks associated with participation are constituted by the possible side effects of mitotane:
- adrenal insufficiency (steroidhormone suppletion starts with mitotane by default)
- gastro-intestinal disturbances
- liver enzyme alterations
- neurological toxicity
- hormone alterations

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

Histologically confirmed diagnosis of ACC.
Low-intermediate risk of relapse defined as: stage I-III ACC(according to the ENS@T

classification 2008).
Microscopically complete resection, defined as no evidence of microscopic residual disease based on surgical reports, histopathology and post-operative imaging.
Ki67 index < or equal 10 %.
Post-operative imaging demonstrating no evidence of disease within 4 weeks before randomization.
ECOG performance status 0-2.
Age equal to or older then 18 years
Adequate bone marrow reserve (neutrophils equal or higher then 1.0 * 10^9/L and/or platelets equal or higher then 80.0 * 10^9/L)
Ability to comply with the protocol procedures
Written informed consent

Exclusion criteria

Time between primary surgery and randomization > 3 months.
Repeated surgery for recurrence of disease.
Renal insufficiency (creatinine clearance <40 ml/min) or liver insufficiency (serum bilirubin >2 times the upper normal range and/ or serum transamininase (AST,ALT)> 3 times the upper normal range).
History of recent or active prior malignancy, except for cured non melanoma skin cancer, cured insitu cervical carinoma, or other treated malignancies where there has been no evidence of disease for at least tree years.
Previous or current treatment with mitotane or other antineoplastic drugs for ACC.
Previous radiotherapy for ACC.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-10-2011
Enrollment:	16
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Lysodren
Generic name:	Mitotane
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	01-11-2010
Application type:	First submission
Review commission:	METC Maxima Medisch Centrum (Veldhoven)
Approved WMO Date:	18-02-2011
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	EUCTR2007-007262-38-NL
ClinicalTrials.gov	NCT00777244
CCMO	NL29842.015.10