Sorafenib as adjuvant to radioiodine therapy in non-medullary thyroid carcinoma

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To investigate whether therapy with the tyrosine kinase inhibitor Sorafenib will increase the accumulation of radioiodine (RaI) and decrease tumor progression in patients with recurrences or metastases of non-medullary thyroid carcinoma with absent...

Ethical review	Approved WMO
Status	Pending
Health condition type	Endocrine and glandular disorders NEC
Study type	Interventional

Summary

ID

NL-OMON31009

Source
ToetsingOnline

Brief title
Sorafenib in Non Medullary Thyroid Carcinoma

Condition

- Endocrine and glandular disorders NEC
- Endocrine neoplasms malignant and unspecified

Synonym
thyroid carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W,Bayer,subsidie Bayer

B.V.

Intervention

Keyword: iodide, radioiodine, sorafenib, thyroid carcinoma

Outcome measures

Primary outcome

The endpoint of the study Part I is the proportion of patients with a favorable response to Sorafenib defined as ONE OR MORE of the following criteria:

1. Reinduction of RaI uptake by RaI scintigraphy: The appearance of one or more RaI accumulating lesions at RaI scintigraphy, planar images and/or SPECT (see below)

2. Serum thyroglobulin levels:

The absence of progression: no statistically significant positive slope at linear regression of the log-transformed serum Tg levels, measured at 0, 4, 8, 12, 16, 20, 24 and 28 weeks after start of Sorafenib:

a. Stable disease: The slope at linear regression of the log-transformed serum Tg levels, measured at 0, 4, 8, 12, 16, 20, 24 and 28 weeks after start of Sorafenib is not significantly different from 0 ln ug/L*time OR

b. Response: The slope at linear regression of the log-transformed serum Tg levels is negative (statistically significantly below 0 ln ug/L*time).

3. CT Imaging:

The absence of progression according to RECIST criteria:

a. Stable disease*neither sufficient shrinkage to qualify for partial response nor sufficient increase to qualify for progressive disease, taking as reference the smallest sum longest diameter since the treatment started.

b. Partial response*at least a 30% decrease in the sum of the longest diameter of target lesions, taking as reference the baseline sum longest diameter;

c. Complete response: the disappearance of all target lesions;

Secondary outcome

The endpoint of the study Part IIa is the proportion of patients with a favorable response to Sorafenib and 6000 MBq RaI with the response in Part I as a reference: defined as ONE OR MORE of the following criteria 6 months after RaI therapy:

a. RaI uptake: A reduction in the number of lesions and/or quantitative RaI uptake in target lesions as assessed by RaI scintigraphy as compared with the diagnostic RaI scintigraphy at 6 months after initiation.

b. Serum thyroglobulin levels: The slope at linear regression of the log-transformed serum Tg levels measured in the 6 months after RaI therapy is statistically significantly different (more negative) than the slope during Part I.

c. CT imaging: Tumor response at imaging according to RECIST criteria is one class higher than during Part I. (for instance: stable disease during Part I and partial response during Part II).

Study description

Background summary

Therapy with radioiodine (RaI) is the only curative therapy in non-medullary thyroid carcinoma. RaI uptake is frequently lost in this disease. Therapy with tyrosine kinase inhibitors may restore the susceptibility to RaI.

Study objective

To investigate whether therapy with the tyrosine kinase inhibitor Sorafenib will increase the accumulation of radioiodine (RaI) and decrease tumor progression in patients with recurrences or metastases of non-medullary thyroid carcinoma with absent or insufficient accumulation of RaI.

Study design

Prospective, open study with patients with recurrences or metastases of differentiated thyroid carcinoma who will undergo 6 months therapy with Sorafenib 800 mg/day. Patients in whom RaI uptake will be restored will be offered high dose (6000 MBq) RaI together with an additional 6 months treatment with Sorafenib. Patients in whom RaI is not be restored but in whom Sorafenib had a favorable effect on tumor growth will be offered continued treatment with Sorafenib.

Intervention

After inclusion, patients will undergo 131I scintigraphy as well as a CT scan. Thereafter, therapy with Sorafenib 800 mg/day will be initiated, and continued during 6 months. After 6 months, 131I scintigraphy and CT scans will be repeated. Serum levels of thyroglobulin will be used as tumormarker.

Study burden and risks

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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

· Patients with non-medullary thyroid carcinoma
· The patients must have undergone total thyroidectomy
· Presence of metastases or inoperable recurrent disease, as proven by elevated serum thyroglobulin levels (Tg) in combination with radiological evidence for tumor.
· No or insufficient RaI uptake in tumor as proven by RaI scintigraphy, performed after prior RaI therapy.

Exclusion criteria

· Pregnancy
· Other active malignancies
· Active kidney, liver or pancreatic disease or dysfunction
· Unstable angina pectoris or recent (<3 months) myocardial infarction.
· Coagulopathy

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)

Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-09-2007
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	Nexavar
Generic name:	Sorafenib
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	29-05-2007
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	EUCTR2007-002365-13-NL
CCMO	NL17727.058.07