Phase II non-randomized study on proton radiotherapy of thymic malignancies

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To investigate te efficacy and the toxicity of protone radiation of thymomas and thymic carcinomas.

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON51962

Source
ToetsingOnline

Brief title
PROTHYM

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
cancer, Thymoma

Research involving
Human

Sponsors and support

Primary sponsor: Swedish Lung Cancer Study Group
Source(s) of monetary or material Support: Maastro

Intervention

Keyword: Phase II, Protone, Radiotherapy, Thymic

Outcome measures

Primary outcome

- Toxicity (e.g. cardiac and pulmonary toxicity)

- Local control at 5 year

Secondary outcome

- PFS

- Overall survival

- Quality of life, measured by EORTC QLQ30 + LC14

- Relapse pattern

Study description

Background summary

Thymic epithelial tumours (TETs or thymic malignancies) which comprise thymoma and thymic carcinoma, are rare cancers worldwide. TETs are heterogenous both morphologically as well as clinically. Thymomas may be associated with a spectrum of autoimmune conditions, whereas this is rare in thymic carcinomas. Thymic carcinomas are more prone to distant metastatic spread.
Surgery remains the cornerstone in the management of TETs. Minimally invasive techniques including thoracoscopic and robotic surgery for early stage disease are gradually increasing. Chemotherapy, although often with a moderate response, has a role in downstaging as well as managing more advanced disease.The role for radiotherapy is a matter of ongoing debate but the use of postoperative radiotherapy (PORT) after incomplete surgery and/or advanced stage (III/IV according to Masaoka) is more or less standard. There is considerably less evidence and weaker consensus for the efficacy of PORT of stage II patients and the use of it varies worldwide.

Radiotherapy with photons for TET patients has been reported feasible and with acceptable toxicity. Treatment is generally given with IMRT-technique and doses in the literature varies between 45 and 60 Gy with 1.8 or 2 Gy/fraction.

Many of the thymoma patients will become long time survivors and thus may suffer from late toxicities such as radiation induced lung disease (RILD) or radiation induced heart disease (RIHD). For many years RIHD has been of major concern when irradiating patients with left-sided breast cancer and Hodgkin*s disease. It includes a wide range of symptoms such as pericarditis, myocardial infarction, valvular heart disease and coronary heart disease. Lately this has become a greater concern when treating thoracic malignancies such as lung and esophageal cancer. Depending on the good prognosis, there is a strong rationale as to try to limit the cardiac dose to the thymoma patients.

Radiotherapy with protons have emerged as a potential possibility to achieve local control and eventually reduce the risk for late toxicity and secondary tumors. From early on, thymic malignancies was recognized as a group who would eventually benefit from proton therapy. Treating thoracic malignancies with protons is cumbersome because of many reasons; tumor and organs at risk motion may result in interplay effects which compromise dose distribution being one of them. Movement of mediastinal structures occurs but seems to be minor compared to the movement in the lung parenchyma and patients with Hodgkins* disease has been successfully treated with protons. TETs are generally located in close proximity to the mediastinum. Recent years more and more data have been published showing superior dose distribution and feasibility regarding toxicity while treating thymomas with protons. The majority of previous thoracic proton therapies have been given with passively-scattered technique. At the Skandion Clinic and at Maastro all patients will be treated with pencil beam scanning (PBS) with proton energies ranging from 60 to 230 MeV. This technique may further optimize dose distribution although planning, quality assurance and motion management is even more crucial.

Study objective

To investigate te efficacy and the toxicity of protone radiation of thymomas and thymic carcinomas.

Study design

This is a multicentre non-randomized phase II study of proton beam radiotherapy in patients with thymic epithelial tumours (i.e. thymoma and thymic carcinoma) in the post-operative setting or in inoperable patients with localized disease. Patients not willing or for any reason unsuitable to undergo proton treatment will be asked to participate in a follow-up assessment after the regular photon treatment in the same manner as the included patients.

Study burden and risks

Burden:

Patiënts who participate in this study will undergo some extra examinations, which consist oft:
- 11 QOL questionnaires
- 17 Extra ECG's
- 3 Extra ultrasounds of the heart
- Bloodtest, done by withdrawing an extra tube of blood during a standard blood withdrawal.

Risks:
- The above mentioned examinations are low-risk

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

- Histological or cytological diagnosis of thymoma or thymic carcinoma
- With radical surgery stage III, IV and selected stage II with type B2, B3 or thymic carcinoma according to local routine
- With non-radical surgery (R1 or R2), stage I - IVa, any histology
- Medically inoperable or patient refusing surgery, stage I - IVa, any histology
- PS WHO 0-2
- FEV1 >/1l or >/40% of predicted and CO diffusion capacity >40% of predicted (post-operative measures)
- Age >/18 years, no upper age limit
- Written informed consent

Exclusion criteria

- Masoaka-Koga stage IVb (distant metastases)
- Pregnancy
- Serious concomittant systemic disorder incompatible with the study
- Tumour motion >0,5cm on two repeated 4DCT

Study design

Design

Study phase:	2
Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	04-07-2022
Enrollment:	10

Type:	Actual

Ethics review

Approved WMO Date:	14-04-2022
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

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
ClinicalTrials.gov	NCT04822077
CCMO	NL78208.068.21