Re-induction of a systemic immune response after initial response with immune therapy with radiotherapy in metastatic or locally recurrent lung cancer

Published: 01-05-2019
Last updated: 10-04-2024

To investigate the progression-free survival after radiotherapy to a single lesion in patients with stage IV non-small cell lung cancer who achieved at least stable disease with immune therapy alone or concurrent immune therapy and chemotherapy and...

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

Summary

ID

NL-OMON50328

Source
ToetsingOnline

Brief title
Remission-Induction

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
lung cancer, Non small cell

Research involving
Human

Sponsors and support

Primary sponsor: MAASTRO clinic
Source(s) of monetary or material Support: MAASTRO clinic

Intervention

Keyword: Immune therapy, Lung cancer, Non small cell, Radiotherapy

Outcome measures

Primary outcome

To investigate the progression-free survival after radiotherapy to a single lesion in patients with stage IV non-small cell lung cancer who achieved at least stable disease with immune therapy alone or concurrent immune therapy and chemotherapy and who show disease progression. The same immune therapy will be continued.

Secondary outcome

- To investigate the remission rate (RECIST 1.1) of the irradiated lesion

- To investigate the remission rate (RECIST 1.1) of the non-irradiated lesion(s)

- To investigate the toxicity of this combination.

- Biobanking for later translational research

- Overall survival

- Immune response to combined radio/immunotherapy (blood-based)

Study description

Background summary

Immune therapy with checkpoint inhibitors have changed the outcome of patients with metastatic non-small cell lung cancer (NSCLC) in first and in second line, with improved progression-free survival (PFS), overall survival (OS) and

quality of life compared to standard chemotherapy. Inhibitors of the PD-1/ PD-L1 axis are now approved for the treatment of patients with metastatic NSCLC in first line or second line treatment.
Radiation has consistently been shown to activate key elements of the immune system. Radiotherapy in combination with different forms of immune therapy such as anti-PD-(L)1, anti-CTLA4,immunocytokines, dendritic cell vaccination and Toll-like receptor agonists improved consistently local tumor control and very interestingly, lead to better systemic tumor control (the *abscopal* effect) and the induction of specific anti-cancer immunity with a memory effect. Moreover, as PD1/PD-L1 is upregulated by radiation and radiation can overcome resistance for PD-(L)1 blockage, their combination is logical.
In small series, it has been shown that a new long-lasting remission can be induced by irradiating one tumor site in patients who showed cancer progression after an initial response to immune therapy alone or concurrent immune therapy and chemotherapy . In these series, the original immune therapy was continued and the treatment was very well tolerated.

Study objective

To investigate the progression-free survival after radiotherapy to a single lesion in patients with stage IV non-small cell lung cancer who achieved at least stable disease with immune therapy alone or concurrent immune therapy and chemotherapy and who show disease progression. The same immune therapy will be continued.

Study design

This is a prospective, single arm phase II trial.

Intervention

Patients continue the same immune therapy they already received and get radiotherapy to one lesion. The lesion may or may not be symptomatic. The preferred radiotherapy dose is 24 Gy in 3 fractions (dosage on the 10 Gy isodose is allowed), but other fractionation schedules (e.g. 30 Gy/ 10 fractions, 20 Gy/ 5 fractions, 20-24 Gy / 1 fraction for SRS) are allowed if these are standard for a certain location or palliative indication in the body.

Study burden and risks

The patients will have some toxicity of radiotherapy. This will be dependent on the dose and of the location of the tumour. However, the radiotherapy is with the exception of stereotactic radiosurgery (SRS) for brain metastases, low dose palliative doses, of which only low to moderate side effects are expected. For SRS, this will be a standard indication because of symptomatic brain metastases progression. The latter patients would receive the same SRS anyway. The

combination of radiotherapy with the checkpoint inhibitors that are used for lung cancer have been investigated in several trials, and no additional toxicity above the two treatment modalities alone has been reported. The risks and side effects of the blood withdrawals (4x) are negligible.

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

- Non small cell lung cancer
- CR, PR or SD initially under immune therapy (possibly combined with chemotherapy)
- Progressive disease
- Able to continue the same immune therapy (i.e. no adverse events grade 3 or

more)

Exclusion criteria

- Patients with any grade 3 or higher toxicity from previous therapy;
- Patients who are not eligible for continuation of the immune therapy according to standard practice;
- Corticosteroids in a dose of at maximum 10mg prednisone or equivalent per day.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-08-2019
Enrollment:	80
Type:	Actual

Ethics review

Approved WMO

Date:	01-05-2019
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Approved WMO

Date:	11-12-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	15-01-2021
Application type:	Amendment
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	NCT03406468
CCMO	NL64034.068.18