Response and Toxicity Prediction by Microbiome analysis in locally advanced NSCLC treated with IO (durvalumab) after Chemoradiotherapy (sequential and concurrent)

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The predictive value of the microbiome (throat swabs and stool samples) to identify patients who will relapse during durvalumab treatment after CRT (False negative Rate) at 6 months. Exploratory endpoints include the effects of antibiotic therapy…

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

Summary

ID

NL-OMON50946

Source
ToetsingOnline

Brief title
PREDICTION trial

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
microbioma, Non small cell lung carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: Astra Zeneca,unrestricted grant van Astra Zeneca

Intervention

Keyword: chemoradiation, microbioma, NSCLC, response

Outcome measures

Primary outcome

Progression of disease defined by regular CT scan and physical examination and

occurrence of toxicity.

Secondary outcome

Changes in circulating immune cells.

Study description

Background summary

Despite the improvements in Overall and Progression Free Survival in patients treated with concurrent or sequential chemoradiotherapy followed by consolidation therapy with PD-1 blockade (durvalumab), a significant number of patients suffer from recurrent disease within one year.
To allow for a more adequate patient follow-up, identification of a biomarker predicting early recurrence or long-lasting disease control is required. The former group could be monitored more closely while the latter can suffice with less outpatient visits and less radiological evaluations. Ineffective therapies can be ceased earlier and allow a switch to a more effective regimen. This seems appropriate since assessment of tumor recurrence after ChemoRT is more complicated due to the ample possibility of non-malignant changes in the lung (radiation pneumonitis or infection). So far, no biomarkers have been identified for this purpose.
Recently, the microbiome has attracted attention for its ability to modify the immune system and thereby changing the immune surveillance in humans. This is considered to be of pivotal importance to sustain a long-lasting tumor control in different tumor types treated with immune checkpoint inhibitors.

Study objective

The predictive value of the microbiome (throat swabs and stool samples) to identify patients who will relapse during durvalumab treatment after CRT (False negative Rate) at 6 months. Exploratory endpoints include the effects of antibiotic therapy before and during IO treatment on toxicity and response rate.
Mass cytometry (CyTOF) of circulating immune cells will be examined in a subset of patients including metabolome analysis.

Study design

This is a prospective observational multicenter study, during 2 years, 126 patients will be included after first inclusion. Patients be included from 2 centers in the Netherlands and 4 centers in Belgium.

Study burden and risks

Collection of stool and throat swipe before start of durvalumab treatment; sampling of blood for analysis of volatile organic compounds. No benefit is foreseen in participation to this study.

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

1. Stages IIIA, IIIB and IIIC (as per UICC 8th TNM edition) NSCLC (histologically or cytologically confirmed) amenable for concurrent chemoradiotherapy according to multidisciplinary tumor board.
2. No signs of disease progression after Chemoradiation (sequential and concurrent)
3. At least 1 cycle of chemotherapy as part of the radiotherapy schedule but no more chemotherapy between last radiotherapy session and start durvalumab
4. Absence of any of following targetable driver mutations: (EGFR, ALK, ROS1)
5. >= 18 years
6. ECOG <= 1
7. Must be willing to provide collected stool samples and allow to obtain a throat swab during the observation period.
8. Demonstrate adequate organ function, all screening labs should be performed within 10 days of start durvalumab

Exclusion criteria

1. Is currently participating in or has participated in a study of an investigational agent or using an investigational device within 4 weeks of the first dose of treatment.
2. Has had prior monoclonal antibody therapy within 4 weeks prior to study Day 1 or who has not recovered (i.e., <= Grade 1 or at baseline) from adverse events due to agents administered more than 4 weeks earlier.
3. Previous treatment with PD-1-PD-L1 axis inhibiting immunotherapy.
4. Active or history of autoimmune disease or immune deficiency,
5. Subjects with a condition requiring systemic treatment with either corticosteroids (> 10 mg daily prednisone equivalents) or other immunosuppressive medications within 14 days of study drug administration
6. Has evidence of symptomatic interstitial lung disease or an active, non-infectious pneumonitis.

Study design

Design

Study type: Observational invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	03-06-2022
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	electronic nose (spironose)
Registration:	No

Ethics review

Approved WMO

Date:	28-02-2022
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	28-04-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO

Date:	21-08-2024
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NCT04711330
CCMO	NL76017.058.21