A randomized phase II study comparing atezolizumab after concurrent chemo-radiotherapy with chemo-radiotherapy alone in limited disease small-cell lung cancer (ACHILES study)

Published: 03-10-2019
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This study has been transitioned to CTIS with ID 2024-515755-37-00 check the CTIS register for the current data. Primary: • To investigate whether adjuvant atezolizumab treatment after standard, concurrent chemo-radiotherapy improves overall...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory tract neoplasms
Study type	Interventional

Summary

ID

NL-OMON49619

Source
ToetsingOnline

Brief title
ACHILES

Condition

- Respiratory tract neoplasms

Synonym
cancer, small-cell longcancer

Research involving
Human

Sponsors and support

Primary sponsor: Norwegian University of Science and Technology
Source(s) of monetary or material Support: Het onderzoek wordt gefinancieerd door de Universiteit voor Wetenschap en Technologie uit Trondheim in Noorwegen.

Intervention

Keyword: Adjuvant, Atezolizumab, Limited disease, Small cell lung cancer

Outcome measures

Primary outcome

OS

Secondary outcome

BRR, PFS, adverse events, quality of life.

Study description

Background summary

Lung cancer is the most common cause of cancer-related deaths. Small-cell lung cancer (SCLC) accounts for approx. 15% of the cases. Untreated, it is a very aggressive disease with a poor prognosis (2-4 months). SCLC metastasizes quickly and more frequently than other types of lung cancer. Up to 90 % of patients respond to therapy, but most experience relapse. Only a few patients are operable at the time of diagnosis. For inoperable disease, chemotherapy (cisplatin plus etoposide) with concurrent radiotherapy is the main treatment for patients with limited disease. Prophylactic cranial irradiation is recommended. The 5-year survival is 25-30%. Thus there is a clear medical need for new and better treatment options. Immunotherapy has been established as both first- and second-line therapy in advanced non-small-cell lung cancer (NSCLC). Immunotherapy is not yet established in the treatment of SCLC, but several studies show promising results, that have led to new research initiatives. In this study we would like to study the effects of the addition of treatment with atezolizumab after standard treatment with chemo-radiotherapy in limited disease SCLC.

Study objective

This study has been transitioned to CTIS with ID 2024-515755-37-00 check the CTIS register

for the current data.

Primary:
• To investigate whether adjuvant atezolizumab treatment after standard, concurrent chemo-radiotherapy improves overall survival (OS) compared with no treatment after standard, concurrent chemo-radiotherapy in limited disease SCLC patients.
Secondary:
• Best response rates (BRR).
• Progression free survival (PFS).
• Toxicity.
• Health related quality of life.

Study design

Phase II, randomized, open-label study.
All participants will be treated with 4 courses of chemotherapy (platinum and etoposide) and 30-40 fractions of radiotherapy (see protocol chapter 4).
Prophylactic cranial irradiation is recommended.
Patients who have completed the chemo-radiotherapy without major delays, who do not show disease progression at the treatment evaluation visit (CT-scan) and who have an adequate performance status will be randomized (1:1) to adjuvant atezolizumab treatment every 3 weeks for 1 year or observation with no treatment (as is the current standard of care).
Study duration 5 years.
Visit frequency during atezolizumab: every 3 weeks for 1 year.
Visit frequency follow-up: year 1-2-3: every 3 months; year 4-5: every 6 months.
160 randomized patients (212 to be included).

Intervention

Treatment with chemo-radiotherapy with or without adjuvant follow-up treatment with atezolizumab.

Study burden and risks

Risk: Adverse effects of study treatment.
Burden:
Screening (2-4 weeks), 4 courses of chemotherapy, 30-40 fractions of radiotherapy, 50% of patients: atezolizumab adjuvant therapy for 1 year.
Treatment:
Etoposide: I.V. infusion 500 mL every 3 weeks (30 min per infusion, day 1-3, 4 cycles)
Cisplatin or carboplatin: I.V. infusion 1.000 mL every 3 weeks (2 h per infusion, day 1, 4 cycles)
Atezolizumab: I.V. infusion 500 mL every 3 weeks (30-60 min per infusion, day

1, 1 year)
Study procedures:
Physical examination: (almost) every cycle; follow-up: 2-4 times/year.
Blood tests: every cycle; follow-up: 2-4 times/year, 10-25 mL per occasion.
MRI brain: during screening (in line with standard treatment).
PET CT-scan: during screening (in line with standard treatment).
CT-scan thorax and abdomen: every 3-6 months (in line with standard treatment).
Tumor biopsy: 0-1.
Pregnancy test (if relevant): every months for 17 months.
Pulmonary function test: 1.
Questionnaires EORTC QLQ-C30 and LC13 : every 3 months for 2,5 years.
Optional: Tumor biopsy at disease progression.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Age >= 18 years.
2. Histologically or cytologically confirmed SCLC
3. Previous radiotherapy to the thorax is allowed as long as the patient can receive TRT of 45-60 Gy.
4. Stage I-III according to TNM v8, ineligible for surgery provided all lesions can be included in a tolerable radiotherapy field (*limited disease*).
5. ECOG performance status 0-2.
6. Measureable disease.
7. Adequate organ function. See protocol chapter 5 for details.
8. FEV1 > 1 L or > 30 % of predicted value and DLCO > 30 % of predicted value.
9. Female patients of childbearing potential should use highly effective contraception. See protocol chapter 5 for details.

Exclusion criteria

1. Prior systemic therapy for SCLC or immune checkpoint blockade therapy.
2. Malignant cells in pericardial or pleural fluid. See protocol chapter 5 for details.
3. Serious concomitant systemic disorders. See protocol chapter 5 for details.
4. Lung disease requiring systemic steroids in doses of >10 mg prednisolone (or equivalent dose of other steroid).
5. Previous allogeneic or organ transplant.
6. Active or history of autoimmune disease or immune deficiency. See protocol chapter 5 for details.
7. History of certain lung diseases. See protocol chapter 5 for details.
8. Live vaccine administered last 30 days, active infection requiring IV antibiotics, active viral hepatitis or HIV.
9. Pregnancy or lactation

Study design

Design

Study phase:	2
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-06-2020
Enrollment:	100
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Carboplatin
Generic name:	Carboplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Cisplatin
Generic name:	Cisplatin
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Etoposide
Generic name:	Etoposide
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Tecentriq
Generic name:	Atezolizumab
Registration:	Yes - NL outside intended use

Ethics review

Approved WMO

Date:	03-10-2019
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO

Date:	21-01-2020
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	19-08-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-09-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	16-10-2020
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	26-03-2021
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	23-02-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	01-04-2022
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	06-07-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam

	(Rotterdam)
Approved WMO Date:	24-10-2023
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	29-01-2024
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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
EU-CTR	CTIS2024-515755-37-00
EudraCT	EUCTR2017-004572-62-NL
CCMO	NL71399.078.19