A prospective, randomized study comparing chemotherapy versus chemotherapy plus immunotherapy in patients with advanced non-small cell lung cancer with low cTML and oncogenic driver,STK11 or KEAP1 mutation and a PD-L1 TPS<50%.

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To compare the objective response rate between patients with metastatic non-small cell lung cancer characterized by PDL-1 TPS

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

Summary

ID

NL-OMON56597

Source
ToetsingOnline

Brief title
OMIT IO

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
non-small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: NFU

Intervention

Keyword: Immunotherapy, NSCLC, Predictive biomarker

Outcome measures

Primary outcome

Objective response rate

Secondary outcome

Clinical benefit rate (defined as the proportion of patients with CR/PR + SD),

progression free survival (PFS), overall survival (OS)

Study description

Background summary

Biomarkers beyond PD-L1 to identify patients with metastatic non-small cell lung cancer that will not derive benefit from treatment with immune checkpoint inhibition are currently lacking. In a retrospective study we uncovered a complex biomarker consisting of low cTML and either STK11, KEAP1 or oncogenic driver mutation that independent of PD-L1 predicted for non response following treatment with single agent immune checkpoint inhibition. Here we propose to validate this biomarker prospectively.

Study objective

To compare the objective response rate between patients with metastatic non-small cell lung cancer characterized by PDL-1 TPS<50% and low cTML (<300 nonsynonymous mutations) and either actionable mutation, inactivating STK11 or KEAP1 mutations, treated by either chemo-immunotherapy or chemotherapy alone.

Study design

Randomized controlled phase II clinical study

Intervention

Patients will receive carboplatin-pemetrexed-pembrolizumab according to the KN189 regimen or the same dose and schedule of carboplatin-pemetrexed

Study burden and risks

The determination of the biomarker to be validated requires an extension of a standard molecular diagnostic laboratory procedure, i.e. is not associated with any risk for the patient. Both carboplatin-pemetrexed-pembrolizumab and carboplatin-pembrolizumab are standard of care regimen whose risk-benefit ratio is well characterized and established. No additional procedures compared to routine management of patients with advanced non small cell lung cancer undergoing systemic treatment will be implemented

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. Age >18 years 2. Advanced, metastatic non-small cell lung cancer UICC stage IV 3. ECOG PS 0-2 4. PDL-1 TPS <50% (Dako 22C3) 5. Low cTML (<300 nonsynonymous mutations) and either actionable mutation, inactivating STK11 or KEAP1 mutations as detected by NGS using OCA+ or TSO500 gene panel. 6. No prior systemic therapy except for patients with activating mutations. 7. Fit for treatment with chemo-immunotherapy deemed by the treating physician. 8. Measurable disease (RECIST 1.1). 9. In case of activating mutation, pretreatment with appropriate (i.e. guideline recommended) targeted therapy is required with demonstrated disease progression.

Exclusion criteria

1. Symptomatic CNS metastasis requiring immediate radiotherapy or neurosurgical intervention.
2. Any contra-indication (as per label) for treatment with immune checkpoint inhibitors.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-01-2024

Enrollment:	162
Type:	Anticipated

Medical products/devices used

Generic name:	Oncomine Comprehensive Assay Plus
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	17-01-2024
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	24-01-2025
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
CCMO	NL82961.000.23