Clinical Performance Study Protocol for Use of the [redacted] PD-L1 [redacted] CDx Assay: Evaluation of PD-L1 Expression Levels in Non-small Cell Lung Cancer Specimens from Phase III Study [redacted]

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The primary objective of this study is to evaluate the clinical performance of the [Redacted] PD-L1 [Redacted] CDx Assay in terms of its ability to identify patients with non-squamous metastatic NSCLC (mNSCLC) who may benefit from treatment with […

Ethical review	Approved WMO
Status	Pending
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON57309

Source
ToetsingOnline

Brief title
[redacted]

Condition

- Other condition
- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lung Cancer, squamous metastatic NSCLC

Health condition

Non-Small-Cell-Lung Cancer (NSCLC)

Research involving
Human

Sponsors and support

Primary sponsor: [redacted]
Source(s) of monetary or material Support: Astra Zeneca,funded by the sponsor;[Redacted]

Intervention

Keyword: in vitro diagnostic assay, Non-Small-Cell-Lung Cancer (NSCLC)

Outcome measures

Primary outcome

The primary efficacy endpoints of the [Redacted] study will also serve as the primary endpoints of this clinical performance study. As such, thisstudy (RD007150) will have 2 dual primary endpoints identical with those listed in the [Redacted] protocol, as well as additional endpoints unique to the RD007150 study.

Dual Primary Endpoints

* Overall survival (OS), defined as the time from randomization until the date of death due to any cause, among all randomized participants.

* Progression-free survival (PFS), defined as the time from randomization until radiological progression [Redacted], or death due to any cause (in the absence of progression), among all randomized participants.

These endpoints will be assessed by the pharmaceutical partner according to the [Redacted] study protocol and the associated [Redacted] Statistical Analysis Plan (SAP).

Primary Acceptance Criteria

The clinical performance of the [Redacted] PD-L1 [Redacted] CDx Assay as a CDx for the identification of patients who may benefit from treatment with rilvegostomig in combination with platinum-based doublet chemotherapy will be considered satisfactory if the primary analysis in study [Redacted] support the efficacy of the investigational medicinal product in the patient population selected using the investigational assay.

Secondary outcome

A secondary endpoint is not defined.

Additionally, the following endpoints will be evaluated among all specimens collected as part of enrollment screening for [Redacted] and tested with the [Redacted] PD-L1 [Redacted] CDx Assay:

* Initial and final overall staining acceptability rate
* Initial and final background acceptability rates
* Initial and final tissue morphology acceptability rates

There are no pre-determined acceptance criteria associated with the additional endpoints.

Study description

Background summary

[Redacted] (detailed in the [redacted] protocol [redacted]) is a phase III, 2-arm, randomized, double-blind, global, multicenter study assessing the efficacy and safety of [redacted] compared with pembrolizumab, both in combination with platinum-based
doublet chemotherapy, as a first-line treatment for patients with non-squamous mNSCLC whose tumors express PD-L1 (tumor cell [TC] >=1%) without known actionable genomic mutations (including but not limited to EGFR, ALK, and ROS1). The scientific rationale for the design of
the [redacted] study is contained in Section 4.2 of the [redacted] protocol [redacted].
Approximately 878 participants will be randomized into the [redacted] study in a 1:1 ratio into the following arms:
* Arm A (experimental): [redacted] in combination with platinum-based doublet chemotherapy, followed by [redacted] in combination with chemotherapy, or
* Arm B (control): pembrolizumab in combination with platinum-based doublet chemotherapy followed by pembrolizumab in combination with chemotherapy

Randomized patients will be stratified [Redacted].

This diagnostic (Dx) study (RD007150) is a clinical performance study being conducted in association with the [Redacted] study. PD-L1 testing (to support patient enrollment into the [Redacted] study) will be performed at designated central laboratories (referred to as Dx testing sites) with the investigational [Redacted] PD-L1 [Redacted] CDx Assay under this Dx protocol. A PD-L1 expression level of >=1% TC, as determined by the [Redacted] PD-L1 [Redacted] CDx Assay, will be one of the inclusion criteria for enrollment into [Redacted]. Additionally, [Redacted] will be one of the stratification factors used for randomization of patients into the treatment arms.

Study objective

The primary objective of this study is to evaluate the clinical performance of the [Redacted] PD-L1 [Redacted] CDx Assay in terms of its ability to identify patients with non-squamous metastatic NSCLC (mNSCLC) who may benefit from treatment with [Redacted] in combination with platinum-based chemotherapy, as part of clinical trial [Redacted].
An additional objective of this Dx protocol is to evaluate the performance of [Redacted] PD-L1 [Redacted] CDx Assay in staining FFPE NSCLC samples on the [Redacted] instrument in a clinical use setting

Study design

[Redacted] is considered a drug (Rx)-diagnostic (Dx) combined trial, which is the simultaneous evaluation of the efficacy and safety of an investigational medicinal therapy ([Redacted] in combination with platinum-based doublet chemotherapy) and the performance evaluation of an investigational in vitro diagnostic (IVD), ie, the [Redacted] PD-L1 [Redacted] CDx Assay.

A PD-L1 tumor cell (TC) expression level >=1% (PD-L1 TC >=1%) will be required for [Redacted] study (Rx) enrollment. the PD-L1 tumor cell expression levels will be determined with the [Redacted] PD-L1 [Redacted] assay (investigational IVD), meaning that the investigational device results will be used for patient selection of the Rx trial. In this context, this is an interventional clinical performance study, where the investigational [Redacted] PD-L1 [Redacted] CDx Assay is being used as a companion diagnostic (CDx) device to identify non-squamous mNSCLC patients who may benefit from treatment with the investigational therapy in the clinical trial. In addition, [Redacted] will be one of the stratification factors to randomize patients into treatment arms.

Stained slides will be interpreted by qualified pathologists, who will assign the PD-L1 expression level (at the 1% and 50% TC thresholds) in accordance with the [Redacted] PD-L1 [Redacted] CDx Assay scoring algorithm and interpretation guide. In addition, for each case, a PD-L1 expression level will also be assigned [Redacted] and [Redacted] will be recorded for exploratory purposes. Performance of the [Redacted] PD-L1 [Redacted] CDx Assay will be evaluated as described in Section 7 of this Dx protocol. In brief, the clinical performance of the investigational IVD device will be measured by its ability to identify the patients who are most likely to benefit
from the investigational therapy. Clinical performance will be considered acceptable if the clinical biomarker-associated efficacy endpoint(s) are met. Thus, the efficacy analyses specified in the pharmaceutical protocol will be used to assess the benefit of the investigational therapy and the effectiveness of the investigational IVD assay for patient selection. In addition, staining performance of the investigational device will be assessed.

Intervention

Lung biopsies will be obtained in the framework of the pharmaceutical study if archival (leftover) samples are not available.
PD-L1 test result is one of the enrollment criteria for the pharmaceutical study.

Study burden and risks

Collection of tissue samples is considered part of standard clinical practice in this tumor indication to enable diagnostic testing in order to determine the most appropriate therapeutic option. If a new tumor biopsy is needed to enable investigational PD-L1 testing, the tissue will be obtained using a medically

routine sampling procedure. Patients will only undergo a new biopsy when risks are considered medically appropriate by their treating physicians. Note that the risk of a patient experiencing at least one complication during the biopsy procedure is ~10%. The mortality rate for elective surgical lung biopsy for patients with interstitial lung disease is <2%.

The risks to patients in both studies include false-positive results, false-negative results, delayed results, unevaluable results/loss of patient sample, and confidentiality breaches.

Contacts

Public
[redacted]

[redacted] [redacted]
[redacted] [redacted]
US
Scientific
[redacted]

[redacted] [redacted]
[redacted] [redacted]
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

All tumor specimens submitted as part of [redacted] that also satisfy the inclusion criteria outlined below, will be tested with the [redacted] PD-L1 [redacted] CDx Assay.

To be eligible for [redacted] PD-L1 [redacted] CDx Assay staining/interpretation under this protocol, a specimen must meet all of the following criteria:
1. It must be an FFPE NSCLC tumor specimen submitted from patients who were screened for enrollment into the [redacted];
2. It must be an FFPE tumor block processed in accordance with standard practice or unstained FFPE slides prepared from such a tumor block if sufficient slides for PD-L1 testing are available; and
3. It must contain sufficient tumor tissue for interpretation at the discretion of the reviewing pathologist

Please refer to [redacted] study [redacted] to review pharmaceutical study population eligibility criteria.

Exclusion criteria

A specimen will be excluded from staining with the investigational assay if any of the following
conditions apply:
1. It is fixed in alcohol-formalin-acetic acid, 95% alcohol, or any other alcohol-based fixative, or PREFER; or
2. It is a fine needle aspirate or a cytology specimen; or
3. It consists of tissue containing bone that has been decalcified;* or
4. Cut slides were prepared from FFPE blocks beyond the cut-slide stability of 12 months prior to staining.

*Prior to testing any bone specimen, evidence of decalcification must be obtained. This information may be obtained from the pathology report. If the pathology report is not available or does not specify whether the sample has been decalcified or not, the sample must be held and the submitting site queried as to whether the sample has been decalcified. If the sample has been decalcified, testing cannot proceed.

Patient exclusion criteria will be listed in the pharmaceutical protocol D702FC00001.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-11-2024
Enrollment:	30
Type:	Anticipated

Medical products/devices used

Generic name:	[redacted] PD-L1 [redacted] CDx Assay
Registration:	No

Ethics review

Approved WMO Date:	07-02-2025
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

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	NL87849.000.24