A Phase I/II, Open-label, Dose Escalation and Dose Expansion Study to Evaluate the Safety, Pharmacokinetics, Pharmacodynamics, and Efficacy of rilvegostomig (AZD2936) Anti-TIGIT/Anti-PD-1 Bispecific Antibody in Participants with Advanced or Metastatic Non-small Cell Lung Cancer (ARTEMIDE-01)

Published: 23-07-2021
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This study has been transitioned to CTIS with ID 2023-508262-15-00 check the CTIS register for the current data. Part D dose expansion:- To assess safety and tolerability of AZD2936 (rilvegostomig) in CPI-naive participants with stage IV NSCLC with...

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

Summary

ID

NL-OMON54261

Source
ToetsingOnline

Brief title
ARTEMIDE-01

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Lungcancer, Non-small cell lungcarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Astra Zeneca
Source(s) of monetary or material Support: AstraZeneca AB

Intervention

Keyword: Anti-TIGIT/Anti-PD-1 Bispecific Antibody, AZD2936 (rilvegostomig), Non-small Cell Lung Cancer

Outcome measures

Primary outcome

Part D dose expansion:

- Percentage of participants at each dose levelwith AEs and imAEs, SAEs,

DLT-like events, vital signs, and abnormal laboratory parameters

- Rate of AZD2936 (rilvegostomig) discontinuation due to toxicity at each dose

level

Secondary outcome

Part D dose expansion:

- According to RECIST v1.1:

• DCR

• DoR

• DRR

• Progression-free survival (PFS)

All parts of the study:

- PK parameters to be evaluated include Cmax, AUC, clearance, and t1/2

- Incidence of anti-drug antibodies (ADAs) against AZD2936 (rilvegostomig) in serum

Exploratory

- Assessment of antitumor activity will be evaluated by measuring and profiling ctDNA changes

- Assessment of changes in tumor- and immune-associated marker profiles will be investigated in peripheral blood and tumor tissue biopsies by DNA, RNA, or protein measures, including but not limited to:

• Changes in the frequency and profile of T-cell populations such as activated/proliferating T cells by flow cytometry (CD8+ Ki67+), by gene expression (IFN-γ and T effector gene signatures), and by IHC (CD8) as well as T cell repertoire by high-throughput sequencing

• Changes in tumor-associated and immune-mediator proteins, including but not limited to serum/plasma levels of chemokines and cytokines (IFN-γ, CXCL9)

- Assessment of baseline tumor- and immune-associated marker profiles will be investigated in peripheral blood and tissue biopsies (tumor or non-tumor) by DNA, RNA, or protein measures, including but not limited to:

• Baseline expression levels of TIGIT, PD-L1, PD-1, CD8 and IFN-γ gene signature in relation to clinical outcomes evaluated by IHC and/or gene expression

• Baseline peripheral immune cell profile and tumor-associated and

immune-mediator proteins in relation to clinical outcomes evaluated by flow

cytometry, high-throughput sequencing and proteomics

• Baseline tumor mutational burden and profile in relation to clinical outcomes

evaluated by high-throughput DNA sequencing

Study description

Background summary

AZD2936 (rilvegostomig) is briefly summarized below. A detailed description of the chemistry, pharmacology, and nonclinical data for AZD2936 (rilvegostomig) is provided in the Investigator*s Brochure.

AZD2936 (rilvegostomig) is a monovalent, bispecific, humanized, IgG1 triple mutant mAb antibody against human PD-1 and TIGIT. AZD2936 (rilvegostomig) was constructed on the backbone of the DuetMab molecule, and its antigen-binding fragment portions are comprised of the variable domains of the anti-TIGIT COM902 antibody and anti-PD-1 LO115 antibody. The IgG1 Fc domain carries the triple mutation (L234F/L235E/P331S) designed to reduce Fc-mediated immune effector functions. In the preclinical studies, dual blockade of TIGIT and PD-1 by AZD2936 enhanced human T cell function and promoted antitumor immune responses.

Study objective

This study has been transitioned to CTIS with ID 2023-508262-15-00 check the CTIS register for the current data.

Part D dose expansion:
- To assess safety and tolerability of AZD2936 (rilvegostomig) in CPI-naive participants with stage IV NSCLC with PD-L1 TPS >= 50%
- To determine the preliminary antitumor activity of AZD2936 (rilvegostomig) in CPI-naive participants with stage IV NSCLC with PD-L1 TPS >= 1%
- T

All parts of the study:
- To assess the PK profile compatibility of AZD2936 (rilvegostomig) with Q3W dosing in 2L+ CPI experienced participants with stage III/IV unresectable NSCLC
- To assess the immunogenicity of AZD2936 (rilvegostomig)

Exploratory

- To assess the preliminary antitumor activity of AZD2936 (rilvegostomig)via circulating biomarkers
- To assess tumor and immunomodulatory associated effects of AZD2936 (rilvegostomig) in 2L+ CPI-experienced participants with stage III/IV unresectable NSCLC
- To evaluate the association of tumor baseline characteristics with the anti-tumor activity of AZD2936 in 2L+ CPI-experienced participants with stage III/IV unresectable NSCLC

Study design

Overall Design
This is a first-time-in-human (FTIH), open-label, multicenter, multi-part, dose-escalation and dose-expansion study to evaluate the safety, PK, pharmacodynamics, and efficacy of AZD2936 (rilvegostomig) in adult participants with stage III unresectable or stage IV NSCLC. The study includes 2 parts: Part A (dose escalation) and Part B (dose expansion). Overall, up to approximately 102 participants will receive treatment with AZD2936 at approximately 35 sites globally.

Part D Dose Expansion: Approximately sixty (60) CPI-naive participants with stage IV NSCLC whose tumors express PD-L1 TPS >= 50%. Participants will be randomized in two different doses (750 mg and 1500 mg)

Intervention

Following an initial screening period of up to 28 days, eligible participants will receive AZD2936 (rilvegostomig) every 3 weeks (Q3W) administered via intravenous (IV) infusion at the selected dose starting on Cycle 1 Day 1 for a maximum of 35 cycles. Participants will be treated with study intervention until disease progression, unacceptable toxicity, investigator*s decision, completion of the maximum of 35 treatment cycles, or withdrawal of consent. All participants will be followed for survival until the end of the study.

No dose reductions of AZD2936 (rilvegostomig) will be allowed at any time. Instructions for dose interruption or discontinuation, and toxicity management for AZD2936-related toxicity, including management of immune-mediated reactions, infusion-related reactions, and non-immune-mediated reactions will be provided in the Toxicity Management Guidelines (provided as an appendix to the protocol).

Study burden and risks

This is the first time AZD2936 (rilvegostomig) will be studied in humans. Therefore, the side effects of AZD2936 (rilvegostomig) and their frequency are not fully known at this time. Possible side effects of AZD2936 (rilvegostomig)

include immune-mediated side effects and infusion reactions.

Extra burden for the patient:
During the first two treatments, the patients are asked to come to the hospital more often. After treatment, there is a follow-up period with visits to the hospital or patients are contacted by telephone.

Contacts

Public
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Disease for part D only:
•Stage IV squamous or non-squamous NSCLC.
•PD-L1 TPS >= 50%
•provision of archival tumor tissue (or fresh tumor tissue biopsy must

be confirmed if archival tumor tissue is not available and if clinically feasible) is mandatory at screening for all study parts
•No sensitizing EGFR mutations or ALK fusions.
•No documented test result for other known genomic alteration for which a targeted therapy is approved in first line per local standard of care (ROS1, NTRK fusions, BRAF, V600E mutation, etc.)

Prior therapy:
•Part D (Dose Expansion): Must meet one of the definitions below:
(i) No prior treatment for NSCLC, and not in need of rapid disease control via chemotherapy-containing regimen, or
(ii) Prior treatment for NSCLC with one regimen consisting of chemotherapy only.
•No unresolved toxicities of >= Grade 2 (CTCAE v5.0) from prior therapy (excluding
vitiligo, alopecia, endocrine disorders that are controlled with replacement hormone
therapy, asymptomatic laboratory abnormalities).

Overall condition:
•ECOG performance status 0 or 1 at enrolment.
•Life expectancy of >= 12 weeks at enrolment.
•Adequate bone marrow, liver and kidney function.

Exclusion criteria

- Participants with either of the following are excluded:
(a) Sensitizing epidermal growth factor receptor mutations or anaplastic lymphoma kinase fusions (documented test result is mandatory for patients with non-squamous histology). For patients with squamous histology mutation, testing is mandatory only
if participant is a never smoker or in the presence of a mixed histology.
(b) Documented test result for any other known genomic alteration for which a targeted therapy is approved in first line per local standard of care (eg, ROS1, NTRK fusions, BRAF, V600E mutation, etc).

- part D only:
Any prior systemic treatment with an immune-oncology agent, including but not limited to anti-PD-1, anti-PD-L1, anti-CTLA-4. Treatment with one previous systemic chemotherapy will be allowed.

- Symptomatic central nervous system (CNS) metastasis.
(a) Note: Participants with known CNS lesions should be asymptomatic, adequately treated with stereotactic radiation therapy, craniotomy, gamma knife therapy, or whole brain radiotherapy, with no subsequent evidence of CNS progression (documented with magnetic resonance imaging [MRI] scans showing the

absence of brain metastasis progression after radiotherapeutic intervention); participants must not require steroid exceeding 10 mg prednisone or 2 mg/day of dexamethasone or equivalent; participants with a history of CNS metastases must have MRI of the brain at screening. Participants with CNS metastases who are receiving steroids must be on a stable dose of steroids for >= 7 days prior to study entry and prior to baseline imaging.

- Thromboembolic event within 3 months before the first dose of investigational product.

- History of organ transplant.

- Active primary immunodeficiency/active infectious disease(s):
(a) Active infection including tuberculosis (TB) (clinical evaluation that includes clinical history, physical examination, and radiographic findings and TB testing in line with local practice).
(b) Human immunodeficiency virus (HIV) (positive for HIV-1 or HIV-2 antibodies).
(c) Chronic or active hepatitis B, chronic or active hepatitis C; however, participants who have chronic hepatitis B and are receiving suppressive antiviral therapy are allowed to be enrolled if alanine aminotransferase (ALT) is normal and viral load is controlled. Controlled hepatitis B viral load is defined as serum hepatitis B virus DNA < 100 U/mL by polymerase chain reaction (PCR). Participants with controlled hepatitis B viral load must remain on antiviral therapy, per institutional practice, during the study treatment and follow-up period to ensure adequate viral suppression. Participants who have chronic hepatitis C are allowed to be enrolled if ALT is normal and hepatitis C virus (HCV) RNA undetectable by PCR, either spontaneously or in response to a successful prior course of anti-hepatitis C therapy (Regev et al, 2020).Controlled hepatitis C viral load is defined as undetectable hepatitis C RNA by PCR
either spontaneously or in response to a successful prior course of anti-hepatitis C therapy.
(d) Acute hepatitis A.
(e) For all participants in the study, all local institutional standards for coronavirus disease 2019 (COVID-19) must be followed for testing. For participants with a known previous COVID-19 infection, either negative PCR test must be documented prior to the first dose or a minimum of 10 days must have elapsed since the last positive COVID-19 test.

- History of arrhythmia (such as multifocal premature ventricular contractions, bigeminy, trigeminy, ventricular tachycardia), which is symptomatic or requires treatment (National Cancer Institute [NCI] CTCAE v5.0 Grade 3); symptomatic or uncontrolled atrial fibrillation despite treatment, or asymptomatic sustained ventricular tachycardia.

- Uncontrolled intercurrent illness including, but not limited to, ongoing or active known infection, cardiomyopathy of any etiology, symptomatic congestive

heart failure (as defined by New York Heart Association class >= 3), ILD, uncontrolled hypertension, uncontrolled diabetes mellitus, unstable angina pectoris, history of myocardial infarction within the past 6 months, serious chronic gastrointestinal conditions associated with diarrhea (eg, active inflammatory bowel disease), active non-infectious skin disease (including any grade rash, urticarial, dermatitis, ulceration, or psoriasis, but excluding stable plaque psoriasis from the definition of active disease), active or prior documented autoimmune or inflammatory disorders requiring chronic treatment with steroids or other immunosuppressive treatment.

- Other invasive malignancy within 2 years prior to screening.

- Psychiatric illness/social situations/substance abuse disorders that would limit compliance with study requirements, substantially increase risk of incurring AEs, or compromise the ability of the participant to give written informed consent.

Prior/Concomitant Therapy
- Current or prior use of immunosuppressive medication within 14 days before the first dose of investigational product is excluded. The following are exceptions to this criterion:
(a) Intranasal, inhaled, topical steroids, or local steroid injections (eg, intraarticular injection).
(b) Systemic corticosteroids at physiological doses not to exceed 10 mg/day of prednisone or equivalent.
(c) Steroids as premedication for hypersensitivity reactions (eg, computed tomography [CT] scan premedication).
(d) Any concurrent chemotherapy, radiotherapy, investigational, biologic, or hormonal therapy for cancer treatment. Concurrent use of hormonal therapy for noncancer-related conditions (eg, insulin for diabetes and hormone replacement therapy) is acceptable.

- Receipt of live attenuated vaccine within 30 days prior to the first dose of study intervention. Note: Participants should not receive live vaccine while receiving study intervention and up to 30 days after the last dose of study intervention. COVID-19 vaccination should not be given for 72 hours prior to administration of the first dose of IP or during the DLT period.

Prior/Concurrent Clinical Study Experience
- Concurrent enrolment into another interventional clinical trial, unless it is an observational (non-interventional) clinical study or during the follow-up period of an interventional study.

- Known allergy or hypersensitivity to AZD2936 or any of the excipients of AZD2936.

Other Exclusions
- Involvement in the planning and/or conduct of the study (applies to both AstraZeneca staff and/or staff at the study site).

- Pregnant or lactating female, or intend to become pregnant during the study.

- Judgement by the investigator that the individual should not participate in the study.

Study design

Design

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	24-12-2021
Enrollment:	18
Type:	Actual

Medical products/devices used

Product type:	Medicine

Ethics review

Approved WMO

Date:	23-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	03-09-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	04-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-02-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	13-05-2022
Application type:	Amendment

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	23-11-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	20-09-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	30-10-2023
Application type:	Amendment
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
EU-CTR	CTIS2023-508262-15-00
EudraCT	EUCTR2021-000857-23-NL
ClinicalTrials.gov	NCT04995523
CCMO	NL78207.056.21