A Multicenter, Phase 1/1b Open-Label, Dose-Escalation Study of ABBV-399, an Antibody Drug Conjugate, in Subjects with Advanced Solid Tumors

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The purpose of this study is to evaluate how safe telisotuzumab vedotin is and how telisotuzumab vedotin is tolerated as monotherapy and in combination with osimertinib.

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

Summary

ID

NL-OMON51611

Source
ToetsingOnline

Brief title
M14-237

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
lungcarcinoma, Non small cell lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: AbbVie B.V.
Source(s) of monetary or material Support: AbbVie

Intervention

Keyword: Advanced/Metastatic, c-MET, EGFR, Non-small Cell Lung Cancer (NSCLC)

Outcome measures

Primary outcome

- Safety and tolerability will be assessed by evaluating adverse events (AE), physical examinations, and changes in laboratory data and vital signs throughout the entire study.

- Blood samples for assay of telisotuzumab vedotin, Total ABT-700 and free MMAE drug levels will be used to evaluate PK parameters. Blood samples for antidrug antibody (ADA) and neutralizing ADA (nADA) will be collected at designated time points throughout the study and ADA/nADA will be correlated with PK and safety outcomes.

Secondary outcome

Secondary:

Objective Response Rate (ORR) (determined using RECIST version 1.1)

Progression-Free Survival (PFS)

Duration of Overall Response (DOR)

Exploratory:

Plasma, serum, and tissues samples (archived/re-biopsy or pre- and on-treatment fresh biopsy and post-progression) will be collected during the study.

Study description

Background summary

Cancer is a condition where cells in a specific part of the body grow and reproduce uncontrollably. Non-small cell lung cancer (NSCLC) is a solid tumor, a disease in which cancer cells form in the tissues of the lung. In many NSCLC and other tumors, there is involvement of a protein known as c-Met, that is often overexpressed on these tumor cells. Telisotuzumab vedotin (ABBV-399 or Teliso-V) is an antibody drug conjugate that specifically targets cancer cells that express c-Met and delivers a cytotoxin to the cancer cell resulting in the death of the cancer cell.

Study objective

The purpose of this study is to evaluate how safe telisotuzumab vedotin is and how telisotuzumab vedotin is tolerated as monotherapy and in combination with osimertinib.

Study design

This is a phase 1/1b open-label, dose-escalation study of telisotuzumab vedotin in subjects with NSCLC.

Intervention

Participants will receive IV telisotuzumab vedotin monotherapy every 2 weeks or IV telisotuzumab vedotin every 2 weeks in combination with osimertinib until meeting the study drug discontinuation criteria.

Study burden and risks

There will be a higher treatment burden for participants in this trial compared to their standard of care. Participants will attend regular visits during the study at a hospital or clinic. The effect of the treatment will be checked by medical assessments, blood tests, computed tomography (CT)/Magnetic Resonance Imaging (MRI) scan, tumor biopsy, checking for side effects and completing questionnaires.

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. Subject must be >= 18 years of age
2. Subject must have advanced NSCLC that is not amenable to surgical resection or other approved therapeutic options that have demonstrated clinical benefit.
-Subjects who have refused, are considered ineligible for or are intolerant of standard therapy are eligible
-Based on evidence gathered in this study or from external sources, the Sponsor in consultation with the Investigators, may decide to limit to specific tumor histology.
- For Monotherapy dose-escalation - Subject with advanced solid tumors
- For Monotherapy dose-expansion and Combination Arms A + D - Subject must have tumor with c-Met overexpression, MET exon 14 skip mutation or MET amplification.
3. Subject has an Eastern Cooperative Oncology Group (ECOG) Performance Status of 0 to 2. For *monotherapy expansion cohort 1.6 Q2W*, subjects have an ECOG performance status of 0 or 1.
4. Subject must have measurable disease per RECIST version 1.1 (Appendix C)
5. Subject has fresh and/or archived diagnostic formalin-fixed paraffin embedded (FFPE) tumor tissue available for analysis
6. Subject has adequate bone marrow, renal, and hepatic function
7. A negative serum pregnancy test for all female subjects of childbearing potential at the screening visit and a negative urine pregnancy test for all female subjects of childbearing potential at baseline prior to the first dose of study drug (for details on contraception refer to Section 5.2.1)

8. Subject is capable of understanding and complying with parameters as outlined in the protocol and able to sign informed consent, approved by an Institutional Review Board (IRB) prior to the initiation of any screening or study-specific procedures.
Additional Inclusion Criteria for Subjects Enrolled on the Combination Therapy Phase
Subjects in the combination therapy arms A and D must meet the above inclusion criteria and be eligible to receive erlotinib, or nivolumab per locally approved labeling, or at the discretion of the Investigator in consultation with the Medical Monitor
-Subjects enrolled in the combination therapy phase Arm E must satisfy the above inclusion criteria numbers 1 - 4, 6 - 8 and the following:
•Subject must have metastatic/locally advanced nonsquamous NSCLC with documented EGFR mutations del19 or L858R, with or without T790M mutation, and none of the EGFR mutations known to be resistant to osimertinib.
•Subject must have received at least 1 but no more than 2 prior regimens, one of which must have contained osimertinib. Subject must have had disease progression while on osimertinib. Only 1 prior regimen may have contained chemotherapy. From amendment 15 and later, and for the purpose of this eligibility criterion, consecutive EGFR TKIs will count as 1 regimen.
• Subject must have available post-osimertinib progression tumor tissue for central c-Met immunohistochemistry (IHC) testing. In cases where it is not possible to obtain a post-osimertinib progression biopsy, archival tissue may be allowed.

Additional Inclusion Criteria for Subjects Enrolled in the *monotherapy expansion cohort 1.6 Q2W*
Subjects must satisfy the above inclusion criteria 1-4 , 6-8, and also the following:
• Subjects must have locally advanced or metastatic, non-squamous, EGFR wild type (site documented EGFR status), c-Met+ (as assessed by an AbbVie designated IHC laboratory) NSCLC. Subjects must not have adenosquamous histology
- Subject must submit archival or fresh tumor material for assessment of c-Met levels during the pre-screening period. Tumor material from the primary tumor site and/or metastatic sites are allowed. If archival tissue is negative for c-Met overexpression, fresh biopsy material may be submitted for reassessment of c-Met expression.
• Subjects must have received no more than 2 lines of prior systemic therapy (including no more than 1 line of systemic cytotoxic chemotherapy) in the locally advanced or metastatic setting.
- Multiple lines of TKIs targeting the same TK count as 1 line of therapy for the purposes of this eligibility criterion.
• Subjects must have progressed on systemic cytotoxic chemotherapy (or are ineligible for systemic cytotoxic chemotherapy) and an immune checkpoint inhibitor (as monotherapy or in combination with systemic cytotoxic chemotherapy, or ineligible for an immune checkpoint inhibitor), and prior anti-cancer therapies targeting driver gene alterations (if applicable).

• Subjects should not have received prior c-Met-targeted antibody-based therapies.

Exclusion criteria

•Subject has received radiation therapy to the lung < 6 months prior to the first dose of ABBV-399.
•Subject has received anticancer therapy including chemotherapy, immunotherapy, biologic, or any investigational therapy within a period of 21 days, or herbal therapy within 7 days prior to the first dose of ABBV-399.
-Palliative radiation therapy for bone or skin metastasis for 10 fractions or less is not subject to a washout period; see below for central nervous system metastatases (CNS).
-For approved targeted small molecules, a washout period of 5 half-lives is adequate (no washout period is required for subjects currently on erlotinib or osimertinib)
•Subject has uncontrolled metastases to the CNS based on head CT or MRI. Subjects with brain metastases may be eligible at least 2 weeks after definitive therapy to all known sites of CNS disease provided they are asymptomatic and either off or on a non-increasing dose (in last 2 weeks) of systemic steroids and not on anticonvulsants for seizure activity directly related to progressive CNS metastases.
• Subjects with a history of interstitial lung disease (ILD) or pneumonitis that required treatment with systemic steroids.
• Subject has evidence of pulmonary fibrosis on screening imaging assessment or any history of pneumonitis or interstitial lung disease (ILD) within 3 months of the planned first dose of the study drug.
• Subject has unresolved clinically significant adverse events >= Grade 2 from prior anticancer therapy except for alopecia or anemia.
•Subject has had major surgery within 21 days prior to the first dose of ABBV-399.
•Subject has a clinically significant condition(s)
•Subject has history of major immunologic reaction to any IgG containing agent.
•Subject has any medical condition which in the opinion of the Investigator or Medical Monitor places the subject at an unacceptably high risk for toxicities.
•Subject is a lactating or pregnant female.
•Subjects with known active COVID-19 infection, subjects with signs/symptoms associated with COVID-19 infection or known exposure to a confirmed case of COVID-19 infection during 14 days prior to Screening: must be screen failed and may only rescreen after they have recovered from COVID-19 or they are no longer considered contagious, per investigator assessment.

Additional Exclusion Criteria for Subjects Enrolled on the Combination Therapy Phase
•Subjects enrolled on the combination therapy phase must satisfy the above

exclusion criteria and also the following:
-Subjects may not receive ABBV-399 in combination with osimertinib, erlotinib, or nivolumab if they have any medical condition which in the opinion of the Investigator places the subject at an unacceptably high risk for toxicities from the combination.
Subjects may not receive nivolumab if they have * Active autoimmune disease with exceptions of vitiligo, type I diabetes mellitus, hypothyroidism and psoriasis
* Used systemic corticosteroids (> 10 mg daily prednisone or equivalent) or other immunosuppressive medications within 14 days of study drug administration, with exception of
inhaled, locally injected or topical steroids
* Known immunosuppressive disease, for example human immunodeficiency virus infection or history of bone marrow transplant or chronic lymphocytic leukemia.
* Prior PD-1 or PD-L1 inhibitor therapy (except as waived by sponsor)

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	09-01-2023
Enrollment:	1
Type:	Actual

Medical products/devices used

Generic name:	c-MET (SP44) IHC Assay
Registration:	No
Product type:	Medicine
Brand name:	Osimertinib
Generic name:	Tagrisso

Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Telisotuzumab Vedotin
Generic name:	Telisotuzumab Vedotin

Ethics review

Approved WMO Date:	03-08-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-10-2022
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-12-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	06-01-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-05-2023
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
EudraCT	EUCTR2014-003154-14-NL
ClinicalTrials.gov	NCT02099058
CCMO	NL81453.000.22