Phase 2, Single-arm, Open-label Study of DS-1062a in Advanced or Metastatic Non-small Cell Lung Cancer with Actionable Genomic Alterations and Progressed On or After Applicable Targeted Therapy and Platinum-based Chemotherapy (TROPION-Lung05)

Published: 30-11-2020
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This study has been transitioned to CTIS with ID 2024-511449-21-00 check the CTIS register for the current data. Primary:To assess the efficacy of DS-1062a, as measured by the ORR, as a treatment for subjects with NSCLC with actionable genomic...

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

Summary

ID

NL-OMON51908

Source
ToetsingOnline

Brief title
DS1062-A-U202 (TROPION-Lung05)

Condition

- Respiratory tract neoplasms

Synonym
Non-Small cell Lung Cancer, NSCLC

Research involving
Human

Sponsors and support

Primary sponsor: Daiichi Sankyo, Inc.
Source(s) of monetary or material Support: industry

Intervention

Keyword: Actionable genomic alterations, Fase 2 study, Metastatic Non-Small Cell Lung Cancer

Outcome measures

Primary outcome

ORR as assessed by BICR per RECIST v1.1.

Secondary outcome

DoR, SoD, DCR, CBR, PFS, TTR as assessed by BICR and by investigator per RECIST

v1.1.

ORR as assessed by investigator per RECIST v1.1.

OS.

Descriptive statistics of safety endpoints.

Plasma concentrations and PK parameters of DS-1062a, total anti- TROP2

antibody, and MAAA-1181a.

Prevalence and incidence of ADA.

Study description

Background summary

DS-1062a is an antibody that has chemotherapy attached to it. DS-1062a is made

to target specific cancer cells, but may affect normal cells. Chemotherapy is a type of cancer treatment that kills cells that grow and divide quickly. This can include cancer cells or normal cells. DS-1062a is designed to bring chemotherapy inside cancer cells that express a protein called trophoblast cell surface protein 2 (TROP2). TROP2 is one of several proteins that are thought to be involved in NSCLC tumortumours. DS-1062a binds to TROP2 to enter the cancer cells and kill them.

Study objective

This study has been transitioned to CTIS with ID 2024-511449-21-00 check the CTIS register for the current data.

Primary:
To assess the efficacy of DS-1062a, as measured by the ORR, as a treatment for subjects with NSCLC with actionable genomic alterations that has progressed on or after 1platinum-containing therapy and 1 platinum-containing therapy and 1 or more lines of targeted therapy to the applicable
genomic alterations in the study.
Secondary:
To further evaluate the efficacy of DS-1062a
To further evaluate the safety of DS-1062a
To assess the PK of DS-1062a
To assess the immunogenicity of DS-1062a

Study design

This is a global, multicenter, single-arm, open-label, Phase 2 study of the efficacy, pharmacokinetics (PK), and safety of DS-1062a in subjects with advanced or metastatic NSCLC with known actionable genomic alterations (ie, alterations in genes with approved therapies, such as EGFR, ALK, ROS1, NTRK, BRAF, MET exon 14 skipping, and RET) andthat has progressed on or after 1 platinum-containing therapy and 1 or more lines of targeted therapy to the applicable genomic alterations in the study. Subjects whose tumors harbor KRAS mutations, in the absence of any of the genomic alterations specified above, will be excluded. Subjects whose tumors harbor EGFR mutations should comprise approximately 50% of subjects enrolled in the study, among those, 80% should have received osimertinib (regardless of T790M status) as a prior line of therapy.
Eligible subjects will receive 6.0 mg/kgof DS-1062a.
The PK of DS-1062a will be evaluated in all subjects. Full PK sampling will be collected from the first approximately 30 subjects with adequate hepatic function and up to 9 subjects with moderate hepatic dysfunction. The remaining subjects will have sparse PK sampling.
The study will be divided into 3 periods: Screening Period, Treatment Period, and Follow-up Period (which includes the Long-term Survival Follow-up [LTSFU]):

• The Screening Period will start on the day of signing the informed consent form (ICF) and will have a maximum duration of 28 days. Rescreening is permitted 1 time for any subject who did not meet reversible or transient eligibility criteria upon initial screening.
• Eligible subjects will enter the Treatment Period, which starts on Cycle 1 Day 1 and continues until a subject permanently discontinues DS-1062a. During the Treatment Period, eligible subjects will receive DS-1062a until they meet one of the discontinuation criteria. Subjects will undergo radiographic assessment of tumor response based on Response Evaluation Criteria in Solid Tumors version 1.1 (RECIST v1.1) by blinded independent central review (BICR) every 6 weeks (± 7 days) from the start of study treatment until radiographic disease progression as assessed by BICR, death, lost to follow-up, or withdrawal of consent. Subjects who discontinue treatment without radiographic disease progression or start new anticancer therapy (without radiographic disease progression will continue to undergo tumor assessments every 6 weeks (±7 days) until radiographic disease progression as assessed by BICR, death, lost to follow-up, or withdrawal of consent. Subjects will continue to receive DS-1062a until radiographic disease progression, clinical progression, unacceptable toxicity, withdrawal of consent by subject, physician decision, protocol deviation, pregnancy, lost to follow-up, study termination by the Sponsor, death, or other reasons. Note: Only protocol deviations that are deemed significant by the investigator, with or without consultation with the Sponsor, may lead to permanent study drug discontinuation.
• The Follow-up Period will start upon permanent discontinuation of DS-1062a. After discontinuing study drug, subjects who have not had radiographic disease progression will continue to be followed for tumor assessments every 6 weeks until radiographic disease progression by BICR. All subjects will be followed every 3 months for survival.

The study start date is the date when the first subject has signed an ICF. A subject is eligible to be enrolled into the study when the investigator or designee has obtained written informed consent, has confirmed all inclusion and exclusion criteria have been met by the subject, and all screening procedures have been completed.

Enrollment is planned to occur over approximately 19 months, with treatment and follow-up (28-day Safety Follow-up and LTSFU) projected to continue for approximately 24 months after the last subject is enrolled. The study will continue until the overall EOS is reached. The anticipated total duration of the study is approximately 43 months.

The primary completion date will occur when all subjects have had either a minimum of 9 months of follow up after start of study treatment or have discontinued from the study, whichever occurs first. This date is used as the data cut-off (DCO) date for the primary analysis. All subjects still on treatment and continuing to derive benefit from DS-1062a at the primary completion date will continue to follow the study schedules of events until the

overall end of study (EOS) is reached. All subjects who have not had disease progression at the time of the primary completion date will continue to be followed for tumor assessments and survival. The subject*s EOS is the date of their last study visit/contact. The overall EOS will occur after the last subject last visit has occurred; or after all subjects have discontinued treatment anddiscontinued from the study, or have died; or an alternative study becomes available for subjects continuing to derive benefit from treatment with DS-1062a
where the drug is offered to these subjects; or the study is discontinued by the Sponsor for other reasons. A final analysis maybe conducted after the overall EOS.

Intervention

DS-1062a drug product will be provided as sterile lyophilized-drug product (Lyo-DP) consisting of 100 mg of lyophilized powder in a single-use amber glass vial to be reconstituted with water for injection and further diluted with 5% dextrose injection prior to use.
DS-1062a will be administered as an intravenous (IV) infusion once every 3 weeks (Q3W) on Day 1 of 21-day cycles at a dose of 6.0 mg/kg. Premedication is required prior to any dose of DS-1062a that must include antihistamines, andacetaminophen with or without glucocorticoids.
If a subject does not experience any IRR during or after the first 2 cycles, the post-infusion observation period can be shortened to at least 30 minutes for subsequent cycles. Subjects with identified IRR related to the study drug should be observed post-infusion for at least 1 hour for the 2 cycles after the IRR event and for at least 30 minutes at each subsequent cycle.

Study burden and risks

The study contains a screening phase, treatment phase and a follow-up phase. Most of the visits will take about 2 to 4 hours, some visits will take between 5 and 7 hours.

The subject will have to undergo several examinations, tests and/or procedures before, during and after his/her treatment. Please refer to the procedure table in the ICF and table 1.1 and 1.2 in section 1 of the protocol for more information.

In addition, questions are asked about the medical history, demographics and eligibility questions.

Subjects will also be tested for HIV and hepatitis. Female patients of childbearing potential will be tested for pregnancy.

Tumour specimen need to be provided (either from current samples or through a

biopsy).

Enrollment is planned to occur over approximately 14 months, with treatment and follow-up (28-day Safety Follow-up and Long-term Survival Follow-up) projected to continue for approximately 24 months after the last subject is enrolled. The study will continue until the overall EOS is reached. The anticipated total duration of the study is approximately 38 months.

The primary completion date will occur when all subjects have had either a minimum of 9 months of follow up after start of study treatment or have discontinued from the study, whichever occurs first.
Possible side effects that are already known are described in the Investigator*s Brochure and the patient informed consent form.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

Has pathologically documented NSCLC that
• Is stage IIIB, IIIC or stage IV NSCLC disease at the time of enrollment (based on the American Joint Committee on Cancer, Eighth Edition).
• Has 1 or more of the following documented activating genomic alterations*: EGFR**, ALK, ROS1, NTRK, BRAF, MET exon 14 skipping, or RET.
* KRAS mutations in the absence of any of the genomic alterations specified above will be excluded.
** Overexpression of EGFR, in the absence of activating mutations, is NOT sufficient for enrollment. Subjects who have not received osimertinib should be evaluated for the presence of EGFR T790M mutation after relapse/progression on/after the most recent EGFR tyrosine kinase inhibitor (TKI), unless the subject is already known to be positive with documented results for this mutation or unless osimertinib is not locally approved.
• Has documentation of radiographic disease progression while on or after receiving the most recent treatment regimen for advanced or metastatic NSCLC.
• Subject must meet the following for advanced or metastatic NSCLC:
• Has been treated with at least 1 but no more than 2 cytotoxic agent-containing therapy in the metastatic setting:
* One platinum-containing regimen (either as monotherapy or combination therapy);
* May have received up to one additional line of cytotoxic agent-containing therapy;
* Those who received a platinum-containing regimen as adjuvant therapy for early stage disease must have relapsed or progressed while on the treatment or within 6 months of the last dose OR received at least one additional course of platinum-containing therapy (which may or may not be same as in the adjuvant setting) for relapsed/progressive disease;
• May have received up to one checkpoint inhibitor (CPI)-containing regimen (may be in combination with a cytotoxic agent as part of a regimen described above or as an additional CPI regimen without a cytotoxic agent);
• Has been treated with 1 or more lines of non-CPI targeted therapy that is

locally approved for
the subject*s applicable genomic alteration at the time of screening; OR one or more of the
agents specified in the table below;
* Those who received a targeted agent for the applicable genomic alterations in the study as
adjuvant therapy for early stage disease must have relapsed or progressed while on the
treatment or within 6 months of the last dose OR received at least one additional course of
targeted therapy for the same genomic alterations (which may or may not be same agent
used in the adjuvant setting) for relapsed/progressive disease.
* Subjects who have been treated with a prior TKI must receive additional targeted therapy,
if clinically appropriate, for the genomic alterations that are considered amenable or the
subject will not be allowed in the study.
• Must undergo a mandatory pre-treatment tumor biopsy procedure.
OR
• If available, a tumor biopsy that was recently collected (within 3 months of screening) after
completion of the most recent anticancer treatment regimen and that has a minimum of
10 × 4 micron sections or a tissue block equivalent of 10 × 4 micron sections may be substituted for
the mandatory biopsy collected during screening.
Note: Results from this biopsy will not be used to determine eligibility for the study.
• Archival tumor tissue from initial diagnosis is required, to the extent that archival tumor tissue is
available.
• Measurable disease based on local imaging assessment using RECIST v1.1.
• Eastern Cooperative Oncology Group performance status (ECOG PS) of 0 - 1 at screening.
• Within 7 days before Cycle 1 Day 1, has adequate bone marrow function defined as:
• Platelet count >=100,000/mm3 (platelet transfusion is not allowed within 1 week prior to
screening assessment).
• Hemoglobin >=9.0 g/dL (red blood cell/plasma transfusion is not allowed within 1 week prior to
screening assessment).
• Absolute neutrophil count >=1500/mm3 (granulocyte-colony stimulating factor [G-CSF]
administration is not allowed within 1 week prior to screening assessment).
(See Section 6.5 and Section 6.7 for use of G-CSF and erythropoietin)

• Within 7 days before Cycle 1 Day 1, has adequate organ function:
• Adequate hepatic function defined as:
* Aspartate aminotransferase (AST)/alanine aminotransferase (ALT) <=2.5 × upper limit of
normal (ULN) or AST/ALT <=5.0 x ULN if transferase elevation is due to liver metastases);
AND
* Total bilirubin (TBL) <=1.5 × ULN (or <3.0 mg/dL in the presence of documented Gilbert*s
Syndrome [unconjugated hyperbilirubinemia]).
OR
• Moderate hepatic dysfunction (a maximum of 9 subjects): TBL >1.5 × ULN and <=3 × ULN and
any AST.
Note: After a maximum of 9 subjects with moderate hepatic dysfunction have been enrolled, subsequent subjects with moderate hepatic dysfunction will be excluded.
• Within 7 days before Cycle 1 Day 1, has adequate renal function, including mild or moderate renal
function, defined as:
• Creatinine clearance >=30 mL/min, as calculated using the Cockcroft-Gault equation.
• Has a left ventricular ejection fraction (LVEF) >=50% by either an echocardiogram (ECHO) or
multiple gated acquisition (MUGA) scan within 28 days before Cycle 1 Day 1.
• Has adequate blood clotting function defined as international normalized ratio/prothrombin time and either partial thromboplastin or activated partial thromboplastin time <=1.5 × ULN within 7 days before enrollment.
• Has an adequate treatment washout period before Cycle 1 Day 1

Exclusion criteria

1. Has spinal cord compression or clinically active central nervous system metastases, defined as untreated and symptomatic, or requiring therapy with corticosteroids or anticonvulsants to control associated symptoms. Subjects with clinically inactive brain metastases may be included in the study.
Subjects with treated brain metastases that are no longer symptomatic and who require no treatment with corticosteroids or anticonvulsants may be included in the study if they have recovered from the acute toxic effect of radiotherapy. A minimum of 2 weeks must have elapsed between the end of whole brain radiotherapy and study enrollment. Note: A computed tomography (CT) or magnetic resonance imaging (MRI) scan of the brain at baseline is required for all subjects. For those subjects in whom central nervous system (CNS) metastases are first discovered at the time of screening, the treating investigator should consider delay of study treatment to document stability of CNS metastases with

repeat imaging at least 4 weeks later (in which case, repeat of all screening activity may be required).
2. Has leptomeningeal carcinomatosis.
3. Had prior treatment with:
a. Any chemotherapeutic agent targeting topoisomerase I, including antibody drug conjugate
(ADC) containing such agent.
b. TROP2-targeted therapy.
4. Uncontrolled or significant cardiovascular disease, including:
a. Mean QT interval corrected for heart rate using Fridericia*s formula (QTcF) >470 milliseconds (msec) (based on the average of screening triplicate 12-lead electrocardiogram determinations).
b. History of myocardial infarction within 6 months prior to Cycle 1 Day 1.
c. History of uncontrolled angina pectoris within 6 months prior to Cycle 1 Day 1.
d. Symptomatic congestive heart failure (CHF) (New York Heart Association Class II to IV) at screening. Subjects with a history of Class II to IV CHF prior to screening must have returned to Class I CHF and have LVEF >=50% (by either an ECHO or MUGA scan within 28 days of Cycle 1 Day 1) in order to be eligible.
e. History of serious cardiac arrhythmia requiring treatment.
f. LVEF <50% or institutional lower limit of normal by ECHO or MUGA scan.
g. Uncontrolled hypertension (resting systolic blood pressure >180 mmHg or diastolic blood pressure >110 mmHg).
5. Has a history of non-infectious interstitial lung disease (ILD)/pneumonitis that required steroids, has current ILD/pneumonitis, or where suspected ILD/pneumonitis cannot be ruled out by imaging at screening.
6. Clinically severe pulmonary compromise resulting from intercurrent pulmonary illnesses including, but not limited to, any underlying pulmonary disorder (ie, pulmonary emboli within 3 months of Cycle 1 Day 1, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion, etc.), or any autoimmune, connective tissue or inflammatory disorders with pulmonary involvement (ie, rheumatoid arthritis, Sjögren's syndrome, sarcoidosis, etc.), or prior pneumonectomy.
7 Clinically significant corneal disease.
8. Has other primary malignancies, except adequately resected non-melanoma skin cancer, curatively treated in situ disease, or other solid tumors curatively treated, with no evidence of disease for >=3 years.

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):	11-08-2021
Enrollment:	13
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	DS-1062a
Generic name:	datopotamab deruxtecan

Ethics review

Approved WMO Date:	30-11-2020
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	19-05-2021
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	17-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-12-2021
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	01-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-02-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	05-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-07-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-08-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	01-10-2022
Application type:	Amendment

Review commission:	METC NedMec
Approved WMO Date:	19-10-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-07-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	08-08-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	17-01-2024
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-01-2024
Application type:	Amendment
Review commission:	METC NedMec

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	CTIS2024-511449-21-00
EudraCT	EUCTR2020-002774-27-NL
ClinicalTrials.gov	NCT04484142
CCMO	NL74951.031.20