Open-Label, Global, Multicenter, Randomized, Phase 3 Study of Sacituzumab Govitecan Versus Docetaxel in Patients With Advanced or Metastatic Non-Small Cell Lung Cancer (NSCLC) With Progression on or After Platinum-Based Chemotherapy and Anti-PD-1/PD-L1 Immunotherapy

Published: 22-12-2021
Last updated: 14-09-2024

This study has been transitioned to CTIS with ID 2024-512148-50-00 check the CTIS register for the current data. To compare the overall survival (OS) of sacituzumab govitecan (SG) versus docetaxel.

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

Summary

ID

NL-OMON53739

Source
ToetsingOnline

Brief title
GS-US-577-6153

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Advanced or metastatic non-small cell lung cancer, Lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Gilead Sciences
Source(s) of monetary or material Support: Gilead Sciences;Inc.

Intervention

Keyword: Docexatal, NSCLC, Phase 3, Trodelvy

Outcome measures

Primary outcome

Primary Objective

• To compare the overall survival (OS) of sacituzumab govitecan (SG) versus

docetaxel.

Primary End Point

• OS is defined as the time from the date of randomization until death due to

any cause in the Intent-to-Treat (ITT) Analysis Set.

Secondary outcome

Secondary Objectives

To compare the effect of SG versus docetaxel on the following:

• Progression-free survival (PFS) as assessed by the investigator per Response

Evaluation Criteria in Solid Tumors (RECIST) Version 1.1.

• Objective response rate (ORR) as assessed by the investigator per RECIST

Version 1.1.

• Duration of response (DOR) as assessed by the investigator per RECIST Version 1.1.

• Disease control rate (DCR) as assessed by the investigator per RECIST Version 1.1.

• Safety and tolerability.

• Quality of life (QOL) using non-small cell lung cancer (NSCLC) Symptom Assessment Questionnaire (NSCLC-SAQ).

Secondary End Points

• PFS is defined as the time from the date of randomization until the date of objective disease progression or death (whichever comes first) as assessed by the investigator per RECIST Version 1.1.

• ORR is defined as the proportion of patients who achieve a complete response (CR) or partial response (PR) that is confirmed at least 4 weeks later as assessed by the investigator per RECIST Version 1.1.

• DOR is defined as the time from the first documentation of CR or PR to the earlier of the first documentation of progressive disease (PD) or death from any cause (whichever comes first) as assessed by the investigator per RECIST Version 1.1.

• DCR is defined as the proportion of patients who achieve a CR, PR, or stable disease (SD) as assessed by the investigator per RECIST Version 1.1.

• Incidence of treatment-emergent adverse events (TEAEs) and clinical laboratory abnormalities.

• Time to first deterioration in shortness of breath domain as measured by

NSCLC- SAQ.

• Time to first deterioration in NSCLC-SAQ total score.

Exploratory Objectives

• To characterize the pharmacokinetics (PK) and immunogenicity of SG.

• To assess disease-related symptoms and health related QOL using EQ 5D 3 level (EQ 5D 3L); NSCLC SAQ; the European Organisation for Research and Treatment of Cancer Quality of Life Questionnaire-Core 30 Version 3 (EORTC QLQ C30 v3); Patient Global Impression of Severity (PGIS); and Patient Global Impression of Change (PGIC).

• To assess and compare treatment-related symptoms using the Patient-Reported Outcomes version of the Common Terminology Criteria for Adverse Events (PRO-CTCAE).

• To assess tumor expression of trophoblast cell surface antigen 2 (Trop-2) as a potential predictive biomarker of response to SG.

• To explore blood and tumor biomarkers that may be associated with response to SG treatment.

Exploratory End Points

• Peak (Cmax) and trough (Ctrough) concentrations over time and antidrug antibodies (ADAs) over time.

• Mean change from baseline of total score and all domains of NSCLC--SAQ not assessed as secondary endpoints..

• Mean change from baseline of all domains of EORTC QLQ-C30 v3.

• The proportion of patients with meaningful change in each QOL domain while on treatment.

• Time to first improvement and time to first deterioration in each QOL domain not assessed as secondary endpoints.

• Frequency, severity, or interference of treatment related symptoms.

• Correlation of clinical response with baseline tumor Trop-2 expression.

• Correlation of clinical response with tumor, tumor microenvironment, and blood biomarkers at baseline and after SG treatment.

• Clearance of circulating tumor DNA upon SG treatment.

Study description

Background summary

Recent advances with cancer therapy have dramatically improved the prognosis of advanced lung cancer. After failure of standard cancer treatments, there are limited treatment options for most patients. The use of single agent chemotherapy is the standard of care for patients with recurring or metastasized NSCLC after failure of standard cancer treatments. The main options for single agent chemotherapy include docetaxel, but novel agents remain a significant unmet medical need in treatment of advanced NSCLC. In previous clinical studies looking at other cancers, the study drug (sacituzumab govitecan; SG) was found to have little harm and was effective. Considering the previous clinical data , SG may potentially benefit patients with advanced lung cancer.

Study objective

This study has been transitioned to CTIS with ID 2024-512148-50-00 check the CTIS register for the current data.

To compare the overall survival (OS) of sacituzumab govitecan (SG) versus docetaxel.

Study design

Study GS-US-577-6153 is an open-label, global, multicenter, randomized, Phase 3 study to compare the efficacy and safety of SG versus docetaxel in patients with advanced or metastatic NSCLC with progression on or after platinum-based chemotherapy and anti-programmed death protein 1 (PD-1)/programmed death ligand 1 (PD-L1) immunotherapy received either in combination or sequentially. Patients with actionable genomic alterations will also be included if they have received prior treatment with an appropriate tyrosine kinase inhibitor (TKI).
Patient participation will include screening, randomization, treatment, and follow-up. Screening will last no longer than 28 days to confirm eligibility and establish disease characteristics prior to randomization and treatment.
Approximately 580 eligible patients will be randomly assigned in a 1:1 ratio to receive either SG (Investigational Arm A) or docetaxel (Control Arm B). Randomization will be stratified based on histology (squamous versus nonsquamous), response to last prior immune therapy received (best response PD/SD vs CR/PR on immune therapy), and if they have received prior therapy for actionable genomic alteration (yes vs no).
The primary endpoint of the study is OS. Secondary efficacy endpoints are PFS, ORR, DOR, and DCR as assessed by the investigator per RECIST Version 1.1; time to first deterioration in NSCLC-SAQ total score; and time to first deterioration in shortness of breath as measured by NSCLC-SAQ. Safety will be assessed by the reporting of adverse events (AEs), assessments of vital signs, laboratory results, and extent of exposure to study drug. Additional QOL assessments will be conducted. Pharmacokinetics, ADA, and various biomarkers will also be assessed.
Patients will receive study drug until PD, death, unacceptable toxicity, or another treatment discontinuation criterion is met. Follow-up will begin at the time of the completion of the end of treatment visit, which will occur 30 days (± 7) after the last dose of study drug. All patients will be followed for survival until 1 of the discontinuation criteria from the study is met.
An independent data monitoring committee will be convened at regular intervals to assess the progress of this study, review safety data, and conduct the interim efficacy analysis.
Following completion of global enrollment, additional patients may be enrolled at sites in mainland China in the China Extension Cohort, to ensure adequate number of Chinese participants are enrolled to meet local regulatory requirements. Those participants enrolled in China after global enrollment is complete will not be a part of the primary analysis for global study. The details on China extension cohort is provided in China-specific amendment.

Intervention

Please refer to table 1 of the Main ICF.

Study burden and risks

Please refer to section E9 of this form.

Contacts

Public
Gilead Sciences

Lakeside Drive 333
Foster City CA 94404
US
Scientific
Gilead Sciences

Lakeside Drive 333
Foster City CA 94404
US

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Patients must meet all of the following inclusion criteria at screening/Day *1 to be eligible for participation in this study (no waivers for patient eligibility will be offered or permitted):
1) Female or male patients, 18 years of age or older, able to understand and give written informed consent
2) Life expectancy of 3 months or more
3) Pathologically documented NSCLC with documented evidence of Stage 4 NSCLC disease at the time of enrollment (based on the American Joint Committee on Cancer, Eighth Edition).

4) EGFR, ALK, and PD-L1 results are required prior to enrollment (see Section 6.3.10). Resulting for other actionable genomic alterations is recommended and to be performed as per local standard of care and availability of targeted treatment. For patients with squamous cell carcinoma, EGFR and ALK testing is optional.
5) Must have progressed after platinum-based chemotherapy in combination with anti-PD-1/PD-L1 antibody OR platinum-based chemotherapy and anti-PD-1/PD-L1 antibody (in either order) sequentially.
• Note: Includes patients who received prior platinum based chemoradiotherapy (with or without maintenance anti PD1/PD L1 antibody) for Stage 3 disease. To be considered to have progressed during or after prior treatment with platinum-based chemotherapy, patients should have either received prior platinum-based chemotherapy in the recurrent/metastatic setting or have experienced disease progression within 6 months of last dose of platinum-based chemotherapy administered as part of concurrent chemoradiation for Stage 3 disease or as neoadjuvant or adjuvant therapy. To be considered to have progressed during or after prior treatment with an anti-PD-1/PD-L1 antibody, patients should have either received this therapy in the recurrent/metastatic setting or have experienced disease progression during *maintenance* treatment following concurrent chemoradiation for Stage 3 disease.
a) No additional treatments are allowed in the recurrent/metastatic setting for patients with no actionable genomic alterations.
b) Patients with EGFR, ALK, or any other known actionable genomic alterations must have also received treatment with at least 1 locally approved and available TKI appropriate to the genomic alteration (see Appendix 8).
c) Documented radiographic disease progression while on or after receiving the most recent treatment regimen for advanced or metastatic NSCLC.
6) Measurable disease based on computed tomography (CT) or magnetic resonance imaging (MRI) as assessed by the investigator in accordance with per RECIST Version 1.1. Tumor lesions situated in a previously irradiated area are considered measurable if progression has been demonstrated in such lesions. Historical images within 28 days of the screening visit may be accepted as a screening image if deemed acceptable in the opinion of the investigator.
7) Eastern Cooperative Oncology Group (ECOG) performance status score of 0 or 1 (Appendix 5) before randomization.
8) Adequate hematologic counts without transfusional or growth factor support within 2 weeks of study drug initiation (hemoglobin >= 9 g/dL, absolute neutrophil count >= 1500/mm3, and platelets >= 100,000/µL).
9) Adequate hepatic function (bilirubin <= 1.5 upper limit of normal [ULN], aspartate aminotransferase and alanine aminotransferase <= 2.5xULN or <= 5xULN if known liver metastases, and serum albumin > 3 g/dL).
• Note: The investigator should follow local practice guidelines and/or the docetaxel label approved in the country of drug administration for assessing eligibility of patients for the study.
10) Creatinine clearance of at least 30 mL/min as assessed by the Cockcroft-Gault equation {Cockcroft 1976}.
11) Male patients and female patients of childbearing potential who engage in

heterosexual intercourse must agree to use protocol-specified method(s) of contraception as described in Appendix 3.

Exclusion criteria

Patients who meet any of the following exclusion criteria at screening/Day *1 are not eligible to be enrolled in this study (no waivers for patient eligibility will be offered or permitted):
1) Mixed small-cell lung cancer and NSCLC histology.
2) Positive serum pregnancy test (Appendix 3) or women who are lactating.
3) Known hypersensitivity to the study drugs, their metabolites, or formulation excipients.
4) Requirement for ongoing therapy with or prior use of any prohibited medications for SG and docetaxel as per Sections 5.6.1 and 5.11, respectively.
5) Received a prior anticancer biologic agent within 4 weeks prior to enrollment or have received prior chemotherapy, targeted small molecule therapy, or radiation therapy within 2 weeks prior to enrollment and have not recovered (ie, > Grade 2 is considered not recovered) from AEs at the time of study entry. Patients participating in observational studies are eligible.
6) Have not recovered (ie, > Grade 2 is considered not recovered) from AEs due to a previously administered agent.
• Note: Patients with any grade alopecia are an exception to this criterion and will qualify for the study.
• Note: If patients received major surgery, they must have recovered adequately from the toxicity and/or complications from the intervention prior to starting study drug.
7) Previously received treatment with any of the following:
a) Topoisomerase 1 inhibitors. Any agent including an ADC containing a chemotherapeutic agent targeting topoisomerase 1
b) Trop-2-targeted therapy
c) Docetaxel as monotherapy or in combination with other agents
8) Active second malignancy
• Note: Patients with a history of malignancy that have been completely treated, with no evidence of active cancer for 3 years prior to enrollment, or patients with surgically cured tumors with low risk of recurrence (eg, nonmelanoma skin cancer, histologically confirmed complete excision of carcinoma in situ, or similar) are allowed to enroll.
9) NSCLC that is eligible for definitive local therapy alone.
10) 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 enrollment, severe asthma, severe chronic obstructive pulmonary disease, restrictive lung disease, pleural effusion, etc); any autoimmune, connective tissue, or inflammatory disorders with pulmonary involvement (ie, rheumatoid arthritis, Sjogren syndrome, sarcoidosis, etc); or prior pneumonectomy.

11) Known active central nervous system (CNS) metastases and/or carcinomatous meningitis. Patients with previously treated brain metastases may participate provided they have stable CNS disease for at least 4 weeks prior to enrollment and all neurologic symptoms have returned to baseline, have no evidence of new or enlarging brain metastases, and are taking 10 mg/day or less of prednisone or its equivalent. All patients with carcinomatous meningitis are excluded regardless of clinical stability.
12) Met any of the following criteria for cardiac disease:
a) Myocardial infarction or unstable angina pectoris within 6 months of enrollment.
b) History of serious ventricular arrhythmia (ie, ventricular tachycardia or ventricular fibrillation), high grade atrioventricular block, or other cardiac arrhythmias requiring antiarrhythmic medications (except for atrial fibrillation that is well controlled with antiarrhythmic medication); history of QT interval prolongation.
c) New York Heart Association Class III or greater congestive heart failure or left ventricular ejection fraction of less than 40%.
13) Active chronic inflammatory bowel disease (ulcerative colitis, Crohn*s disease) or gastrointestinal perforation within 6 months of enrollment.
14) Active serious infection requiring antibiotics.
15) Positive HIV 1 or HIV-2 antibody with detectable viral load OR taking medications that may interfere with SN 38 metabolism.
16) Positive for hepatitis B surface antigen. Patients who test positive for hepatitis B core antibody will require hepatitis B virus DNA by quantitative polymerase chain reaction for confirmation of active disease.
17) Positive hepatitis C antibody and detectable hepatitis C viral load.
18) Other concurrent medical or psychiatric conditions that, in the investigator*s opinion, may be likely to confound study interpretation or prevent completion of study procedures and follow up examinations.

Study design

Design

Study phase:	3
Study type:	Interventional
Intervention model:	Parallel
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	12-09-2022
Enrollment:	16
Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	docetaxel
Generic name:	Taxotere
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Sacituzumab govitecan
Generic name:	Trodelvy

Ethics review

Approved WMO Date:	22-12-2021
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	09-03-2022
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	15-04-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-04-2022
Application type:	Amendment

Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	21-07-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	25-07-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	01-10-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	17-11-2022
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	29-01-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	23-05-2023
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	03-05-2024
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	CTIS2024-512148-50-00
EudraCT	EUCTR2021-003578-30-NL
CCMO	NL79682.028.21