A Phase 1 Study Evaluating the Safety, Tolerability and Pharmacokinetics of Tarlatamab in Subjects With Small Cell Lung Cancer (DeLLphi-300)

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This study has been transitioned to CTIS with ID 2023-506541-39-00 check the CTIS register for the current data. Monotherapy (Parts A, B*, D, E, F and G)Primary Objectives - Evaluate the safety and tolerability of Tarlatamab - Part A only: Determine...

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

Summary

ID

NL-OMON54787

Source
ToetsingOnline

Brief title
20160323

Condition

- Respiratory tract neoplasms

Synonym
oat-cell carcinoma, Small Cell Lung Cancer, small-cell carcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Amgen

Source(s) of monetary or material Support: Amgen

Intervention

Keyword: First-in-Human, Phase 1, Small Cell Lung Cancer

Outcome measures

Primary outcome

Monotherapy:

For all indications:

Primary Endpoints • Dose limiting toxicities (DLTs), treatment-emergent adverse events (AEs), treatment-related AEs, and clinically significant changes in vital signs, ECG, physical examinations, and clinical laboratory tests

Combination Therapy:

Primary Endpoints:

For subjects with RR SCLC who progressed or recurred following at least 1 platinum based regimen:

o DLTs), treatment-emergent AEs, treatment-related AEs, and clinically significant changes in vital signs, ECG, physical examinations, and clinical laboratory tests

Please see protocol section 1 for more information.

Secondary outcome

Monotherapy:

Secondary Endpoints

- Objective Response (OR) per modified Response Evaluation Criteria in Solid

Tumors (RECIST) 1.1

- Duration of Response (DOR)

- Time to response (TTR)

- Progression-Free Survival (PFS)

- Overall Survival (OS)

For subjects with ED SCLC with ongoing clinical benefit following no more than 6 cycles of platinum-based chemotherapy only:

- Relapse Free Survival (RFS)

Combination Therapy:

Secondary Endpoints:

For subjects with RR SCLC who progressed or recurred following at least 1 platinum based regimen:

o PK parameters for Tarlatamab following intravenous administration including but not limited to Cmax, Cmin, AUC over the dosing interval, accumulation following multiple dosing, and, if feasible, t1/2

o OR per modified RECIST 1.1

o DOR

o TTR

o PFS

o OS

Please see section 1 of the protocol for more information.

Study description

Background summary

Small Cell Lung Cancer (SCLC), accounting for 10-15% of lung cancer (Rudin et al, 2015), is an aggressive lung cancer subtype with neuroendocrine differentiation and strongly associated with smoking (Koinis et al, 2016). It displays a distinct natural history characterized by a high growth fraction, rapid doubling time and early establishment of widespread metastatic lesions (Gustafsson et al, 2008). While 30% of patients present with disease confined to one hemithorax [limited disease (LD)], the majority of cases have disease not encompassed by one radiotherapy field [extended disease (ED)]. SCLC is exquisitely sensitive to first-line chemotherapy (approximately 60%-70% response rates) and to radiation which is stark contrast to subsequent resistance to second-line and subsequent therapies after disease recurrence (Byers et al, 2015). Patients with ED develop drug resistance and die as a result of disease at a median time of 10 to 12 months from diagnosis (Rudin et al, 2015). For patients with ED SCLC, first-line treatment is platinum-based chemotherapy. Most patients in the United States receive platinum-etoposide (EP) chemotherapy (with either carboplatin or cisplatin), and some patients receive platinum-irinotecan as an alternative, especially outside the United States. After relapse, topotecan is the only second-line drug approved by the US Food and Drug Administration (FDA). However, despite its indication in this setting, topotecan has produced disappointing response rates (Byers et al, 2015).

Study objective

This study has been transitioned to CTIS with ID 2023-506541-39-00 check the CTIS register for the current data.

Monotherapy (Parts A, B*, D, E, F and G)
Primary Objectives
- Evaluate the safety and tolerability of Tarlatamab
- Part A only: Determine the MTD or RP2D of Tarlatamab

Secondary Objectives
• Evaluate preliminary anti-tumor activity of Tarlatamab
• Characterize the pharmacokinetics of Tarlatamab

Exploratory Objectives
- Evaluate immunogenicity of Tarlatamab

- Evaluate protein, nucleic acid and cellular biomarkers in blood pre and post Tarlatamab treatment (eg cytokines, lymphocyte status, CTCs)
- Evaluate relationship of baseline target protein expression in tumor tissue, tumor microenvironment characteristics and clinical benefit
- Evaluate the effects of chemotherapy and time elapsed post chemotherapy on *T cell fitness* (Part B only)
- Evaluate relationship of cytokine release syndrome (CRS) mitigation strategies and the incidence of CRS (Part D only)

Combination Therapy (Part C)
Primary Objectives
For subjects with RR SCLC who progressed or recurred following at least 1 platinum based regimen:
• Evaluate the safety and tolerability of Tarlatamab when administered in combination with pembrolizumab
• Determine the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D) of Tarlatamab in combination with pembrolizumab

Secondary Objectives
For subjects with RR SCLC who progressed or recurred following at least 1 platinum based regimen:
• Characterize the PK of Tarlatamab when administered in combination with pembrolizumab
• Evaluate preliminary anti-tumor activity of Tarlatamab in combination with pembrolizumab

Please refer to protocol section 1 for more information.

Study design

This is an open-label, ascending, multiple dose, phase 1 study evaluating Tarlatamab monotherapy and in combination with anti PD1 therapy in subjects with SCLC. Tarlatamab will be administered (with or without step dosing) as a short term IV infusion as part of a 4-week cycle Parts A-F, and as part of a 3-week cycle in Part G.

The study will consist of 7 parts:
• Part A (monotherapy): For subjects with RR SCLC who progressed after at least 1 platinum-based regimen, which includes 2 phases: (A1) Dose Exploration and (A2) Dose Expansion. Part A3 will be conducted in China to confirm Part A1 MTD/RP2D.
• Part B (monotherapy): For subjects with ED SCLC with ongoing clinical benefit following no more than 6 cycles of platinum-based chemotherapy. Part B was planned to commence once MTD or RP2D is identified in Part A in subjects with RR SCLC. Part B will not be opened.
• Part C (combination with anti PD1 therapy): Tarlatamab in combination with anti-PD1 therapy for subjects with RR SCLC who progressed after at least 1

platinum-based regimen which includes: Dose exploration of Tarlatamab in combination with fixed dose of pembrolizumab
• Part D (evaluation of additional CRS mitigation strategies): Tarlatamab monotherapy for subjects with RR SCLC who progressed after at least 1 platinum-based regimen. To mitigate the risk of CRS, one or more of the following prophylactic measures may be implemented (during cycle 1 only): IV hydration, additional corticosteroid prophylaxis with oral dexamethasone, administration of tocilizumab prophylaxis, etanercept prophylaxis, or acetaminophen prophylaxis.
• Part E (Tarlatamab administration with 24-hour monitoring): This cohort will allow for subjects to have Tarlatamab administered in inpatient or at outpatient infusion centers with 20 to 24 hours monitoring for cycle 1 doses.
• Part F (Tarlatamab 8-hour outpatient cohort): In Part F, up to 30 subjects will be enrolled to evaluate the safety and tolerability of Tarlatamab when administered in outpatient infusion centers with 8-hour monitoring for cycle 1 doses (discharge between 6-8 hours is acceptable.
• Part G (Tarlatamab alternative dosing schedule cohort[s]): This part will explore different dosing schedules of Tarlatamab in subjects with RR SCLC.

The dose exploration phases of the study Part A1 will estimate the MTD or RP2D of Tarlatamab using a Bayesian logistic regression model (BLRM; Neuenschwander et al, 2008). Once a RP2D has been determined for Tarlatamab monotherapy in Part A1, this will be followed by dose expansion phase (Part A2) to confirm the RP2D and to obtain further safety and efficacy data.

Please see protocol section 3.1 for more information.

Intervention

Tarlatamab will be administered as an IV infusion for 60 minutes followed by a flush at dose levels detailed in Table 1-1 and 1-2 of the protocol.

Study burden and risks

The risks and potential side effects of Tarlatamab and the procedures performed in this study are fully described in the Informed Consent Form. Tarlatamab may cause all, some, or none of the side effects listed below. These side effects can be mild but could also be serious life-threatening or even result in death. Because this is the first time Tarlatamab is being given to humans, it is unknown if the patient will have any side effects. Side effects, such as pituitary changes were seen in animals. The meaning of these findings to humans is uncertain. Disadvantages of participation in the study may be: • The additional time it will take • Additional or longer hospital stays • Additional tests • Instructions the patient needs to follow • possible side effects / complications of study related tests or procedures • possible adverse effects /

discomforts from the study drug It is uncertain if taking part in this study will be beneficial for the patient. The condition may get better but it could stay the same or even get worse. The information from this study might help in the development of additional treatments for Small Cell Lung Cancer. [Information on the risks associated with the study participation can be found in Q E9 of this form]

Contacts

Public
Amgen

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NL
Scientific
Amgen

Minervum 7061 Minervum 7061
Breda 4800DH
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

Subject has provided informed consent prior to initiation of any study-specific activities/procedures • Age > 18 years old at the time of signing the informed consent • Histologically or cytologically confirmed SCLC: o Parts A, C, D, E, F and Part G: RR SCLC who progressed or recurred following at least 1

platinum-based regimen; Note: Subjects with a diagnosis of combined small cell carcinoma with predominant small cells (as determined by the local pathologist) may be considered for inclusion in the dose escalation phase of part A based on investigator discretion and after discussion with the medical monitor o Part B: ED SCLC with ongoing clinical benefit (stable disease [SD], partial response [PR], or complete response [CR]) following no more than 6 cycles of first-line platinum-based chemotherapy with the last dose of chemotherapy greater then equal to 28 days prior to the study day 1 (first-line consolidation setting). Part B will not be opened. • Eastern Cooperative Oncology Group (ECOG) performance status of 0-2 • Minimum life expectancy of 12 weeks • RR SCLC only: at least 2 measurable lesions as defined per modified RECIST 1.1 within 21 days prior to the first dose of Tarlatamab. Subjects with 1 measurable lesion may be considered for inclusion after discussion with the Medical Monitor. • Subjects with treated brain metastases are eligible provided they meet the following criteria: o Definitive therapy was completed at least 2 weeks prior to the first dose of Tarlatamab. o There is no evidence of radiographic CNS progression following definitive therapy and by the time of study screening. Patients manifesting progression in lesions previously treated with stereotactic radiosurgery may still be eligible if pseudo progression can be demonstrated by appropriate means and after discussion with the medical monitor. o Any CNS disease is asymptomatic for at least 7 days (unless symptoms are deemed irreversible by the investigator), the patient is off steroids for at least 7 days (physiologic doses of steroids are permitted), and the subject is off or on stable doses of anti-epileptic drugs for malignant CNS disease for at least 7 days. Please refer to section 4.1 of the protocol.

Exclusion criteria

History of other malignancy within the past 2 years prior to first dose of Tarlatamab except: o Malignancy (other than in situ) treated with curative intent and with no known active disease present for > 2 years before first dose of Tarlatamab and felt to be at low risk for recurrence by the treating physician. o Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease. o Adequately treated in situ cancer without evidence of disease. o Prostatic intraepithelial neoplasia without evidence of prostate cancer o Adequately treated urothelial papillary noninvasive carcinoma • Major surgery within 28 days of first dose Tarlatamab • Untreated (includes new lesions or progression in previously treated lesions) or symptomatic brain metastases and leptomeningeal disease • Myocardial infarction and/or symptomatic congestive heart failure (New York Heart Association > class II) within 12 months of first dose of Tarlatamab • History of arterial thrombosis (eg, stroke or transient ischemic attack) within 12 months of first dose of Tarlatamab • Subject with symptoms and/or clinical signs and/or radiographic signs that indicate an acute and/or uncontrolled active systemic infection within 7 days prior to the first dose of investigational product administration

• Prior anti-cancer therapy: at least 28 days must have elapsed between any prior anti-cancer therapy and first dose of Tarlatamab

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	23-07-2019
Enrollment:	10
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	AMG 757
Generic name:	Tarlatamab
Product type:	Medicine
Brand name:	Keytruda
Generic name:	Pembrolizumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO

Date:	22-11-2018
Application type:	First submission
Review commission:	METC NedMec

Approved WMO Date:	31-01-2019
Application type:	First submission
Review commission:	METC NedMec
Approved WMO Date:	15-03-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	10-05-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-09-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	02-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-10-2019
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-01-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-02-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	23-04-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	14-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	22-05-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	27-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	31-08-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	07-09-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-11-2020
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	03-02-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	16-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	17-04-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	15-07-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	12-08-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	24-09-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-03-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	13-04-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	11-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	25-05-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO	

Date:	10-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	28-06-2022
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	14-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	26-01-2023
Application type:	Amendment
Review commission:	METC NedMec
Approved WMO Date:	21-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-06-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	16-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	29-08-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO	

Date:	14-09-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	02-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-11-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-02-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	14-03-2024
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	CTIS2023-506541-39-00
EudraCT	EUCTR2017-003421-15-NL

Register	ID
ClinicalTrials.gov	NCT03319940
CCMO	NL66035.031.18