A Phase 1b Study Evaluating the Safety, Tolerability, Pharmacokinetics and Efficacy of Delta-like Protein 3 Half-life Extended Bispecific T-cell Engager AMG 757 in Subjects with De Novo or Treatment Emergent Neuroendocrine Prostate Cancer

Published: 04-01-2021
Last updated: 07-09-2024

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON51934

Source
ToetsingOnline

Brief title
20200040

Condition

- Other condition
- Prostatic disorders (excl infections and inflammations)

Synonym

Neuroendocrine Prostate Cancer, Prostate Cancer

Health condition

neuro-endocriene prostaatkanker

Research involving
Human

Sponsors and support

Primary sponsor: Amgen
Source(s) of monetary or material Support: Amgen

Intervention

Keyword: bispecific T-cell engager (BiTE®) antibody construct, Delta-like ligand 3 (DLL3), Neuroendocrine Prostate Cancer (NEPC)

Outcome measures

Primary outcome

1. Treatment-emergent adverse events, treatment-related adverse events, and

changes in vital signs, electrocardiogram (ECG), and

clinical laboratory tests

2. Dose limiting toxicities (DLTs)

Secondary outcome

1. o Objective response (OR) per Response Evaluation Criteria in Solid Tumors

(RECIST) 1.1

o Duration of response (DOR) per RECIST 1.1

o Radiographic Progression-free survival (PFS) per Prostate Cancer Working

Group 3 (PCWG3)

o Overall survival (OS)

o Disease Control Rate (DCR) per RECIST 1.1

2. PK parameters for tarlatamab following intravenous (IV) administration

including, but not limited to, maximum serum concentration (Cmax), minimum

serum concentration (Cmin), area under the concentration-time curve (AUC) over

the dosing interval, accumulation ratio, and half-life (t1/2)

Study description

Background summary

Tarlatamab (AMG 757) is a half-life extended (HLE) bispecific T cell engager (BiTE®) antibody designed to direct T-effector cell to DLL3 expressing cells. Currently, a first in human phase 1 study evaluating the safety, tolerability and pharmacokinetics of tarlatamab in subjects with SMLC (Study 20160323) is ongoing. Tarlatamab demonstrated potent cell killing against DLL3 expressing SCLC and other neuroendocrine tumor cell lines in vitro, including the NEPC cell line, NCI-H660.

A detailed description of the chemistry, pharmacology, nonclinical pharmacokinetics, and toxicology of tarlatamab is provided in the tarlatamab Investigator*s Brochure.

Please refer to section 2.2 of the protocol.

Study objective

This study has been transitioned to CTIS with ID 2024-513316-10-00 check the CTIS register for the current data.

Primary:
• To Evaluate the safety and tolerability of tarlatamab
• Determine the maximum tolerated dose (MTD) or recommended phase 2 dose (RP2D)

Secondary:
• Evaluate anti-tumor activity of tarlatamab as assessed by additional measures
• Characterize the pharmacokinetics (PK) tarlatamab

Study design

This is an open label phase 1b study evaluating tarlatamab monotherapy. Tarlatamab will be administered as a short-term IV infusion Q2W (with step

dosing) in a 28-day cycle as monotherapy in subjects with de novo or treatment-emergent NEPC.
The study will consist of 2 parts: dose exploration (Part 1) and dose expansion (Part 2).

Intervention

Tarlatamab will be administered as a short-term IV infusion Q2W (with step dosing) in a 28-day cycle as monotherapy

Study burden and risks

Please refer to section E2 and E9.

Contacts

Public
Amgen

Minervum 7061
Breda 4817 ZK
NL
Scientific
Amgen

Minervum 7061
Breda 4817 ZK
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

o Adult subjects (>= 18 years of age) with metastatic de novo or treatment-emergent NEPC
defined as one or more of the following will be eligible to enroll:
histological diagnosis of
small cell NEPC, prostate carcinoma with neuroendocrine differentiation as defined by
positive immunohistochemical staining for chromogranin and/or synaptophysin in the
majority of the tumor sample or >= 2 alterations in Tp53, RB1, and/or PTEN by immunohistochemistry (IHC) or genomic analyses of baseline tumor tissue or circulating
tumor DNA (ctDNA).
o Subjects are required to have progressed on at least 1 line of prior treatment, including a platinum containing regimen for de novo NEPC (if at the time of
NEPC diagnosis they had no prior diagnosis or treatment for prostate carcinoma) or an
androgen signaling inhibitor (eg, abiraterone, enzalutamide, and/or apalutamide) if
treatment-emergent (had a previous diagnosis of prostate carcinoma prior to NEPC diagnosis).
o Subjects must have measurable disease per Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 criteria with Prostate Cancer Working Group 3 (PCWG3)
guidelines, have an Eastern Cooperative Oncology Group (ECOG) performance status of
<= 2, and adequate organ function.

For a full list of eligibility criteria, please refer to Section 5.1 to Section 5.2 of the protocol.

Exclusion criteria

-History of other malignancy within the past 2 years
-Untreated (includes new lesions or progression in previously treated lesions) or symptomatic brain metastases and leptomeningeal disease
-History or presence of relevant CNS pathology such as uncontrolled epilepsy or seizure disorder, aphasia, paresis, dementia, severe brain injuries, Parkinson*s disease, cerebellar disease, organic brain disorder, or psychosis
-Myocardial infarction within 12 months of study day 1, symptomatic congestive heart failure (New York Heart Association > class II), unstable angina, or clinically significant uncontrolled cardiac arrhythmia

-History of arterial thrombosis (eg, stroke or transient ischemic attack) within 12 months of first dose of tarlatamab

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	22-03-2022
Enrollment:	3
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	Tarlatamab
Generic name:	AMG757

Ethics review

Approved WMO Date:	04-01-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-07-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek

	(Assen)
Approved WMO Date:	13-08-2021
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:	08-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	09-03-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	21-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	02-11-2022

Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-08-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-11-2023
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	CTIS2024-513316-10-00
EudraCT	EUCTR2020-003508-15-NL
ClinicalTrials.gov	NCT04702737
CCMO	NL75623.056.20