A Phase 1b, Master Protocol Evaluating the Safety, Tolerability, Pharmacokinetics, and Efficacy of Sotorasib (AMG 510) in Subjects With Advanced Solid Tumors With KRAS p.G12C Mutation (CodeBreak 101)

Published: 14-12-2021
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This study has been transitioned to CTIS with ID 2023-506794-35-00 check the CTIS register for the current data. - Primary Objective:To evaluate the safety and tolerability of investigational regimens of sotorasib in adult subjects with KRAS p.G12C...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Other condition
Study type	Interventional

Summary

ID

NL-OMON53961

Source
ToetsingOnline

Brief title
20190135 - CodeBreaK 101

Condition

- Other condition
- Malignant and unspecified neoplasms gastrointestinal NEC

Synonym
cancer, Deadly tumors

Health condition

colorectaal kanker / pancreas kanker

Research involving
Human

Sponsors and support

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

Intervention

Keyword: AMG 510, cancer, investigational, Safety

Outcome measures

Primary outcome

Dose-limiting toxicities, treatment-emergent adverse events, treatment related adverse events, and clinically significant changes in vital signs, electrocardiograms (ECGs), and clinical laboratory tests

The primary analysis for this study will occur when target enrollment is complete and each subject either completes at least 6 months on study or withdraws from the study.

The final analysis will be conducted and reported following the end of the study. The end of study date is defined as the date when the last subject across all sites is assessed or receives an intervention for evaluation in the study (ie, last subject last visit), including any additional parts in the study (eg, long*term follow*up), as applicable.

Secondary outcome

Pharmacokinetic parameters of product(s) including, but not limited to, maximum

plasma concentration (Cmax), time to maximum plasma concentration (tmax), and area under the plasma concentration-time curve (AUC)

Objective response rate (complete response [CR] + partial response [PR]), disease control rate (DCR), duration of response (DOR), and progression-free survival (PFS), measured by computed tomography (CT) or magnetic resonance imaging (MRI) and assessed per Response Evaluation Criteria in Solid Tumors Version 1.1 (RECIST 1.1).

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Study description

Background summary

The rat sarcoma (RAS) proto-oncogene has been identified as an oncogenic driver of tumour growth in both non small-cell lung cancer (NSCLC) and colorectal cancer (CRC). Of the genes in the RAS family the KRAS is known to be the most frequently mutated in most cancers.
The KRAS mutation occurs in approx. 13% of lung carcinoma and less than 5% of other solid tumour cancers.
There have been many therapies developed in recent years but because the KRAS mutation is hard to target there is a need to not only develop targeted treatments for those presenting with this muation in their cancer but also to identify these patients to be able to develop targeted therapies.

Sotorasib is a small molecule that irreversibly inhibits the KRAS G12C mutation. It binds with other cells in the cancer tumour and stops cell growth in the cells that harbour KRAS p.G12C mutations. Data collected so far suggests therapeutic benefit to patients with KRAS p.G12C driven cancers. As well as the anti-cancer activity Sotorasib is recorded as being safe and well-tolerated in research studies to date, is being investigated as a first-line treatment option to treat those patients with NSCLC KRAS p.G12C mutation.
Recent developments in the design of drug trials are becoming difficult to capture in a traditional protocol design. Due to this Amgen considers this study, 20190135, a master protocol using the platform design; study multiple targeted therapies in the context of a single disease in a perpetual manner with therapies allowed to enter or leave based on a decision algorithm. Suing this approach Amgen hope to identify the most promising regime of Sotorasib for further clinical research in an efficient and expedited manner.

Study objective

This study has been transitioned to CTIS with ID 2023-506794-35-00 check the CTIS register for the current data.

- Primary Objective:

To evaluate the safety and tolerability of investigational regimens of sotorasib in adult subjects with KRAS p.G12C mutant advanced solid tumors

- Secondary Objectives:

To characterize PK of product(s) used in investigational regimens of sotorasib in adult subjects with KRAS p.G12C mutant advanced solid tumors.
To evaluate anti-tumor activity of investigational regimens of sotorasib in adult subjects with KRAS p.G12C mutant advanced solid tumors

Study design

This study (Subprotocol H) is part of CodeBreaK 101 Master protocol study evaluating various sotorasib investigational regimens in advanced solid tumors with KRAS p.G12C mutation. The Master protocol consists of individual subprotocols that describe the details of the specific sotorasib investigational regimen being evaluated. Subjects will be assigned for screening in a non-randomized fashion to the individual subprotocols based on investigator*s discretion. There is no overarching comparator arm within the master protocol. Each of the individual subprotocols describe the design elements associated with the evaluation of the specific sotorasib investigational regimen(s).

See section on "aanvullende opmerkingen" in this ABR-form for the applicable

cohorts for the Netherlands.

Intervention

AMG 510 (sotorasib) in combination with other medication / therapy:
- Panitumumab
- Panitumumab plus FOLFIRI
- Panitumumab plus FOLFOX

Study burden and risks

Please refer to section E2 and E9.

Contacts

Public
Amgen

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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

For the full list of inclusion criteria please refer to section 5.1 of the subprotocols.

All subprotocols:
• Pathologically documented, metastatic colorectal cancer / metastatic pancreatic cancer with KRAS p.G12C mutation identified through molecular testing. KRAS p.G12C mutation must be identified by an approved diagnostic device for detection of KRAS p.G12C in NSCLC or be performed in a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory.
• Measurable disease per RECIST 1.1 criteria (Section 11.8)
• Eastern Cooperative Oncology Group (ECOG) Performance Status of <= 2
• Life expectancy of > 3 months, in the opinion of the investigator
• Ability to take oral medications and willing to record daily adherence to investigational product
• Corrected QT interval (QTc) <= 470 msec for women and <= 450 msec for men (based on average of screening triplicates
• Adequate hematological laboratory assessments, as follows:
- Absolute neutrophil count (ANC) >= 1.5 x 109/L
- Platelet count >= 100 x 109/L
- Hemoglobin >= 9 g/dL
• Adequate renal laboratory assessments, as follows:
- Estimated glomerular filtration rate based on Modification of Diet in Renal Disease (MDRD) calculation >= 60 ml/min/1.73 m2

Exclusion criteria

For the full list of exclusion criteria please refer to section 5.2 of the subprotocols.

All sub protocols
• History or presence of hematological malignancies unless curatively treated with no evidence of disease >= 2 years
History of other malignancy within the past 2 years, with the following exceptions:
- Malignancy treated with curative intent and with no known active disease present for >2 years before enrollment and felt to be at low risk for recurrence by the treating physician.
- Adequately treated non-melanoma skin cancer or lentigo maligna without evidence of disease.
- Adequately treated cervical carcinoma in situ without evidence of disease.
- Adequately treated breast ductal carcinoma in situ without evidence of disease.

- Prostatic intraepithelial neoplasia without evidence of prostate cancer.
- Adequately treated urothelial papillary non-invasive carcinoma or carcinoma in situ.
• Myocardial infarction within 6 months of study day 1, symptomatic congestive heart failure (New York Heart Association > class II), unstable angina, or cardiac arrythmia requiring medication
• GI tract disease causing the inability to take oral medication, malabsorption syndrome, requirement for IV alimentation, uncontrolled inflammatory GI disease (eg, Crohn's disease, ulcerative colitis)
• Exclusion of hepatitis infection based on the following results and/or criteria:
- Positive Hepatitis B Surface Antigen (HepBsAg) (indicative of chronic Hepatitis B or recent acute hepatitis B)
- Negative HepBsAg with a positive for hepatitis B core antibody (Hepatitis B core antibody testing is not required for screening, however if this is done and is positive, then hepatitis B surface antibody [antiHBs] testing is necessary. Undetectable anti-HBs in this setting would suggest unclear and possible infection and needs exclusion).
- Positive Hepatitis C virus antibody: Hepatitis C virus RNA by polymerase chain reaction (PCR) is necessary. Detectable Hepatitis C virus RNA suggests chronic hepatitis C
• Known positive test for HIV
• Has an active infection requiring systemic therapy
• Received radiation therapy to the lung that is > 30 Gy within 6 months of the first dose of trial treatment

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	09-02-2023
Enrollment:	3

Type:	Actual

Medical products/devices used

Registration:	No
Product type:	Medicine
Brand name:	-
Generic name:	Fluorouracil (5-FU)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	Irinotecan
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	-
Generic name:	Leucovorin (Folinic acid)
Registration:	Yes - NL intended use
Product type:	Medicine
Brand name:	Lumykras
Generic name:	Sotorasib
Registration:	Yes - NL outside intended use
Product type:	Medicine
Brand name:	Vectibix
Generic name:	Panitumumab
Registration:	Yes - NL intended use

Ethics review

Approved WMO Date:	14-12-2021
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-03-2022

Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	08-05-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-05-2022
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:	20-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)

Approved WMO Date:	26-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	28-04-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	05-07-2023
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	25-01-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	19-04-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	03-05-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	10-06-2024
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-06-2024
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	CTIS2023-506794-35-00
EudraCT	EUCTR2020-004721-23-NL
ClinicalTrials.gov	NCT04185883
CCMO	NL79714.056.21