A PHASE 2 STUDY OF FUTIBATINIB IN PATIENTS WITH SPECIFIC FGFR ABERRATIONS

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Cohorts A nd B :The primary objective is to evaluate the objective response rate (ORR) in patients with solid tumors harboring FGFRrearrangements or gastric cancer (including GEJ cancer) harboring FGFR2 amplifications based on independent central…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON52617

Source
ToetsingOnline

Brief title
TAS-120-202

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
solid tumor

Research involving
Human

Sponsors and support

Primary sponsor: Taiho Oncology, Inc.
Source(s) of monetary or material Support: pharmaceutical industry

Intervention

Keyword: FGFR, Futibatinib, phase 2

Outcome measures

Primary outcome

Cohorts A and B

ORR, defined as the proportion of patients experiencing a best overall response of partial response (PR) or complete response (CR) (per Response Evaluation Criteria in Solid Tumors, Version 1.1 [RECIST 1.1]), based on IRC

Cohort C

Complete response rate defined as the proportion of patients who achieved a CR

Secondary outcome

Cohorts A and B : Secondary Endpoints

DOR defined as the time from the first documentationof response (CR or PR per RECIST 1.1 based on IRC) to the first documentation of objective tumor progression or death due to any cause, whichever occurs first, based on IRC

* ORR, defined as the proportion of patients experiencing a best overall response of partial response of PR or CR (per RECIST 1.1), based on Investigator assessment

* DCR, defined as the proportion of patients experiencing a best overall response of stable disease (SD), PR, or CR (per RECIST 1.1), based on IRC

* PFS, defined as the time from first dose of study drug to the date of death

(any cause) or disease progression (based on IRC), whichever occurs first

* OS, defined as the time from the date of first dose to the death date

Safety based on reported AEs and on-study laboratory parameters, graded according to the National Cancer Institute*Common Terminology Criteria for Adverse Events, Version 5.0 (NCI-CTCAE V5.0).

Cohort C

ORR, defined as the proportion of patients who achieved a CR, CRi, or PR

* CR+CRi rate, defined as the proportion of patients who achieved a CR or CRi

* CCyR rate, defined as the proportion of patients who achieved CCyR

* PCyR rate, defined as the proportion of patients who achieved PCyR

* Duration of CR defined as the time from the first documentation of CR to the first documentation of objective tumor progression or death due to any cause, whichever occurs first

* Duration of CR+CRi defined as the time from the first documentation of CR/CRi to the first documentation of objective tumor progression or death due to any cause, whichever occurs first

* DOR defined as the time from the first documentation of CR, CRi, or PR to the first documentation of objective tumor progression or death due to any cause, whichever occurs first

* PFS, defined as the time from first dose of study drug to the date of death (any cause) or disease progression, whichever occurs first

* Relapse-free survival (RFS), defined as the time from the first documentation of CR to the first documentation of disease relapse or death due to any cause,

whichever occurs first.

* Event-free survival (EFS) (leukemia presentation only), defined as the time

from first dose of study drug to treatment failure, disease relapse after CR,

or patient death from any cause.

* OS, defined as the time from the date of first dose to the death date.

* Safety based on reported AEs and on-study laboratory parameters, graded

according to the NCI-CTCAE V5.0

Study description

Background summary

Fibroblast growth factor receptor (FGFR) signaling plays a crucial role in cancer cell proliferation, migration, angiogenesis, and survival. Recent studies have uncovered increasing evidence that deregulated FGFRs can function as driving oncogenes in certain tumor types, maintaining the malignant properties of cancer cells. When FGFRs are amplified, rearranged, or undergo fusion, aberrant activation of downstream pathways results in mitogenic, mesenchymal, and antiapoptotic responses in cells.
Therefore, FGFRs are attractive targets for therapeutic intervention in cancer treatment. This Phase 2 clinical trial will investigate the efficacy, safety, tolerability, pharmacokinetics (PK), and pharmacodynamics of futibatinib in patients with tumors harboring specific FGFR aberrations.

Study objective

Cohorts A nd B :The primary objective is to evaluate the objective response rate (ORR) in patients with solid tumors harboring FGFR rearrangements or gastric cancer (including GEJ cancer) harboring FGFR2 amplifications based on independent central review of radiologic images (IRC).
Cohort C: The overall objective of Cohort C is to assess the clinical activity of futibatinib as monotherapy in the treatment of patients with myeloid/lymphoid neoplasms (MLN) harboring FGFR1 rearrangements.

Study design

Phase 2 study with futibatininb in patients with gastric or gastroesophageal

junction (GEJ) cancer harboring FGFR2 amplification; and patients with myeloid or lymphoid neoplasms harboring FGFR1 rearrangements

Intervention

Patients should visit the clinics and be willing to receive their study drug according to the dosing schema. Furthermore their data of Medical history and demographic data will be collected. They must undergo physicial and vital signs examinations. Radiology scans are performed to exam the tumor status. Tumor biopsies, Blood and urine will be collected.

Study burden and risks

Based on available preclinical and clinical data to date, the Sponsor concludes that the benefit risk assessment results of futibatinib support the continued enrollment and treatment of patients in clinical trials and supports further investigation of futibatinib in tumors with FGF R aberrations.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

1. Provide documented informed consent
2. >=18 years of age (or meets the country's regulatory definition for legal adult age, whichever is greater)
3. Eastern Cooperative Oncology Group (ECOG) performance status 0 or 1
4. Has recovered from the acute toxic effects of prior anticancer therapy to baseline or Grade 1 (except toxicities which are not clinically significant such as alopecia)
5. Known FGFR aberration status and tumor type that meet all of the criteria for one of the following cohorts:
a. Cohort A
I. Histologically-confirmed, locally-advanced, advanced, or metastatic solid tumors harboring a FGFR1-4 rearrangement determined in tumor tissue using next-generation sequencing (NGS), fluorescence in situ hybridization (FISH), or other assays that can determine gene rearrangements in tumor tissues. Patients with primary brain tumor or iCCA are not eligible.
ii. Measurable disease per RECIST 1.1
iii. Had disease progression/recurrence after standard treatment for their advanced or metastatic cancer
b. Cohort B
I. Histologically-confirmed, locally-advanced, advanced, or metastatic gastric or GEJ adenocarcinoma harboring a FGFR2 amplification. The tumor must have an FGFR2/CEN10 ratio of >=5 or an FGFR2 copy number >=10 signals per cell determined in tumor tissue using NGS, FISH, or other assays that can determine gene amplification in tumor tissues.
ii. Measurable disease per RECIST 1.1
iii. Received at least 2 prior systemic regimens for advanced/metastatic disease
iv. Experienced disease progression/recurrence during or after the most recent prior systemic treatment for advanced/metastatic gastric or GEJ cancer
c. Cohort C
I. Confirmed MLN with a FGFR1 rearrangement as defined by WHO criteria
ii. Not a candidate for hematological stem cell transplant (HSCT) or relapsed after HSCT and donor lymphocyte infusion, and progressed and not a candidate for other therapies

6. Has archival or fresh tumor tissue (preferably in block format) for Cohorts A and B and bone marrow tissue for Cohort C available to send to central laboratory.
7. Adequate organ function as defined by the following criteria:
a. Cohorts A and B:
I. Absolute neutrophil count (ANC) >= 1.0 x 10^9/L
ii. Platelet count >= 75,000/mm3 (>= 75 x 10^9/L)
iii. Hemoglobin >= 9.0 g/dL
iv. Alanine aminotransferase (ALT) and aspartate aminotransferase (AST) <= 3.0 × upper limit of normal (ULN); if liver function abnormalities are due to underlying liver metastasis, AST and ALT <= 5.0 × ULN.
v. Total bilirubin <= 1.5 × ULN, or <= 3.0 × ULN for patients with Gilbert's syndrome.
vi. Creatinine clearance (CrCl) (calculated or measured value): >=40 mL/min. For calculated CrCl, use the Cockcroft-Gault formula (Section 6).
vii. Phosphorus <1.5 ULN
b. Cohort C
I. ALT and AST <= 3.0 × ULN; if liver function abnormalities are due to underlying liver metastasis, AST and ALT <= 5.0 × ULN.
ii. Total bilirubin <= 1.5 × ULN, or <= 3.0 × ULN for patients with Gilbert's syndrome.
iii. CrCl (calculated or measured value): >=40 mL/min. For calculated CrCl, use the Cockcroft-Gault formula (Section 6).
iv. Phosphorus <1.5 ULN
8. Women of child-bearing potential (WOCBP) must have a negative serum pregnancy test prior to administration of the first dose of futibatinib. Female patients are not considered to be of child-bearing potential if they are post-menopausal, defined as no menses for 12 months without an alternative medical cause or permanently sterile (hysterectomy, bilateral salpingectomy, or bilateral oophorectomy).
9. Both males and females of reproductive potential must agree to use effective birth control during the study prior to the first dose and for 90 days after the last dose or longer based on local requirements.
10. Ability to take medications orally (feeding tube is not permitted).
11. Willing and able to comply with scheduled visits and study procedures.

Exclusion criteria

1. Currently receiving an investigational drug in a clinical trial or participating in any other type of medical research judged not to be scientifically or medically compatible with this study. If a patient is currently enrolled in a clinical trial involving non-approved use of a device, then agreement with the investigator and the Sponsor's Medical monitor is

required to establish eligibility.
2. History and/or current evidence of any of the following disorders:
a. Non-tumor related alteration of the calcium-phosphorus homeostasis that is considered clinically significant in the opinion of the Investigator
b. Ectopic mineralization/calcification including, but not limited to, soft tissue, kidneys, intestine, or myocardia and lung, considered clinically significant in the opinion of the Investigator
c. Retinal or corneal disorder confirmed by retinal/corneal examination and considered clinically significant in the opinion of the Investigator.
3. Corrected QT interval using Fridericia's formula (QTcF) >470 msec. Patients with an atrioventricular pacemaker or other condition (for example, right bundle branch block) that renders the QT measurement invalid are an exception and the criterion does not apply.
4. Treatment with any of the following within the specified time frame prior to the first dose of futibatinib:
a. Major surgery within 4 weeks (surgical incision should be fully healed)
b. Radiotherapy for extended field within 4 weeks or limited field radiotherapy within 2 weeks
c. A drug that has not received regulatory approval for any indication within 14 or 21 days of treatment for a nonmyelosuppressive or myelosuppressive agent, respectively.
5. Received strong inhibitors or inducers of CYP3A4 within 2 weeks of first dose
6. Prior treatment with an FGFR inhibitor
7. A serious illness or medical condition(s) including, but not limited to, the following:
a. Known acute systemic infection
b. Myocardial infarction, severe/unstable angina, or symptomatic congestive heart failure within the previous 6 months
c. History or current evidence of uncontrolled ventricular arrhythmia
d. Chronic diarrhea diseases considered to be clinically significant in the opinion of the Investigator
e. Congenital long QT syndrome, or any known history of torsade de pointes, or family history of unexplained sudden death
f. Other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or futibatinib administration, or may interfere with the interpretation of study results, and in the judgment of the Investigator would make the patient inappropriate for entry into this study
8. Active central nervous system (CNS) metastasis and/or carcinomatous meningitis. Patients with previously treated brain metastases that are clinically and radiologically stable (for at least 4 weeks prior to enrollment) are eligible.
9. Known additional malignancy that is progressing or has required active treatment within the past 2 years. Patients with basal cell carcinoma of the skin, squamous cell carcinoma of the skin, or carcinoma in situ (eg, breast carcinoma, cervical cancer in situ) that have undergone potentially curative therapy are not excluded.

10. Pregnant or breastfeeding.

Study design

Design

Study phase:	2
Study type:	Interventional
Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	18-12-2020
Enrollment:	12
Type:	Actual

Medical products/devices used

Product type:	Medicine
Brand name:	TAS-120
Generic name:	Futibatinib

Ethics review

Approved WMO Date:	29-04-2020
Application type:	First submission
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	31-07-2020
Application type:	First submission

Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	17-11-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	16-12-2020
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	14-10-2021
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-04-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	27-06-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	22-07-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO Date:	12-10-2022
Application type:	Amendment
Review commission:	BEBO: Stichting Beoordeling Ethiek Bio-Medisch Onderzoek (Assen)
Approved WMO	

Date:	20-10-2022
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
EudraCT	EUCTR2019-004084-49-NL
ClinicalTrials.gov	nct04189445
CCMO	NL73545.056.20