A Phase 2, Open-Label, Single-Arm, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Advanced/Metastatic or Surgically Unresectable Cholangiocarcinoma Including FGFR2 Translocations Who Failed Previous Therapy

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Ethical review	Not approved
Status	Will not start
Health condition type	Gastrointestinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON44339

Source
ToetsingOnline

Brief title
INCB 54828-202

Condition

- Gastrointestinal neoplasms malignant and unspecified

Synonym
bile duct cancer, Cholangiocarcinoma

Research involving
Human

Sponsors and support

Primary sponsor: Quintiles
Source(s) of monetary or material Support: Incyte Corporation

Intervention

Keyword: Cholangiocarcinoma, FGFR2, INCB054828, Phase 2

Outcome measures

Primary outcome

The primary endpoint of this study is to determine the objective response rate (ORR) in subjects with FGFR2 translocations based on the central genomics laboratory results. Objective response rate is defined as the proportion of subjects who achieved a complete response (CR; disappearance of all target lesions) or a partial response (PR; *30% decrease in the sum of the longest diameters of target lesions) based on RECIST version 1.1. Clinical response will be determined by an independent radiological review committee.

Secondary outcome

* ORR in subjects with fibroblast growth factor (FGF)/FGFR alterations other than FGFR2 translocations (Cohort B).

* ORR in all subjects with FGF/FGFR alterations (Cohorts A and B).

* Progression-free survival (PFS = first dose to progressive disease [PD] or death; all cohorts).

* Duration of response (DOR = time from the date of CR or PR until PD; all

cohorts).

* Disease control rate (DCR = CR + PR + stable disease; all cohorts).

* Overall survival (OS = first dose to death of any cause; all cohorts).

* Safety and tolerability will be assessed by evaluating the frequency,

duration, and severity of adverse events; through review of findings of

physical examinations, changes in vital signs, and electrocardiograms; and

through clinical laboratory blood and urine sample evaluations (all cohorts).

* Population pharmacokinetics (all cohorts).

Study description

Background summary

INCB054828 is an inhibitor of the fibroblast growth factor receptor (FGFR) family of receptor tyrosine kinases that is proposed for the treatment of advanced malignancies. Aberrant signaling through FGFR resulting from gene amplification or mutation, chromosomal translocation, and ligand-dependent activation of the receptors has been demonstrated in multiple types of human cancers. Fibroblast growth factor receptor signaling contributes to the development of malignancies by promoting tumor cell proliferation, survival, migration, and angiogenesis. Incyte is proposing to study INCB054828 for the treatment of advanced/metastatic or surgically unresectable Cholangiocarcinoma including FGFR2 translocations who failed previous therapy.

Study objective

The primary objective of this study is to evaluate the efficacy of INCB054828 in subjects with advanced/metastatic or surgically unresectable cholangiocarcinoma with fibroblast growth factor receptor (FGFR) 2 translocation who have failed at least 1 previous treatment.

Secondary Objectives are:
* To evaluate the efficacy of INCB054828 in subjects with advanced/metastatic or surgically unresectable cholangiocarcinoma with different molecular subgroups.

* To evaluate the safety of INCB054828 in subjects with advanced/metastatic or surgically unresectable cholangiocarcinoma.
* To identify and evaluate covariates that may influence the pharmacokinetics of INCB054828 in this subject population through population pharmacokinetic analysis. Additionally, exposure-response analyses for key efficacy and safety parameters will also be considered if sufficient data are available.

Exploratory Objectives:
* To evaluate pharmacodynamics.
* To explore potential biomarkers.
* To evaluate the impact of INCB054828 on quality of life.

Study design

This is an open-label monotherapy study of INCB054828.

Intervention

INCB054828 will be self-administered as a QD oral treatment on a 21-day cycle. Subjects will take study drug for 2
weeks continuously (14 days) followed by a 1-week (7 days) break. The starting dose will be 13.5 mg. Each dose of
study drug should be taken immediately upon rising or after a 2-hour fast. Subjects should plan to fast for 1 additional
hour after taking study drug.

Study burden and risks

Based on an expected average participation of approximately 6 months, the study entails around 16 visits including
physical examinations (i.e. eye exam, vital signs, weight assessment),12 venapunctions, 4 CT-scans and 13 ECGs.
Patients have to take study drug immediately after waking up or 2 hours before eating and not eat for 1 hour after
taking study drug, and follow a diet.
A quality of life questionnaire will be answered.
Subjects will be tested on hepatitis B and C, HIV and pregnancy.
Patient or partner should not get pregnant during the study.
Patient should protect him/herself from sunlight.
There is a risk of the following side effects:

* Hyperphosphatemia - an increase in phosphate levels in the blood and the kidney's inability to get rid of the
increased levels of phosphate (a component of bone and other tissues). Please report any symptoms of
hyperphosphatemia such as muscle cramps, twitching, or mouth numbness or

tingling
* Fatigue (feeling tired)
* Dry mouth
* Alopecia (hair loss and/or thinning)
* Diarrhea (loose, watery bowel movement)
* Stomatitis (redness and sores in your mouth and/or throat)
* Anemia (low hemoglobin levels in blood)
* Dehydration (not enough water in your body)
* Decreased appetite
* Dysgeusia (sense of taste is off)
* Blurred vision
* Weight decreased
* Constipation (cannot have or difficulty having bowel movement)
* Cough
* Epistaxis (nose bleeds)
* Nausea
* Pain in extremity
* Abdominal pain
* Aspartate aminotransferase increased (increase in a type of liver enzyme)
* Back pain
* Dry eye
* Dyspnea (shortness of breath)
* Hyponatremia (low sodium levels in the blood)
* Hypophosphatemia (low phosphate level in the blood)
* Musculoskeletal pain
* Pneumonia
* Vomiting
* Alanine aminotransferase increased (increase in a type of liver enzymes)
* Ascites (accumulation of fluid between the lining of the abdomen and organs)
* Dyspepsia (impaired digestion)
* Hypercalcemia (high calcium level in the blood)
* Hypoesthesia (reduced sense of touch)
* Hypoalbuminemia (low albumin levels in blood)
* Hypokalemia (low potassium in blood)
* Pain
* Paronychia (infection of the nails)
* Upper respiratory tract infection
* Vitamin D deficiency
* Wheezing
For further information on potential risks see section 1.3 of the protocol.

There is no guarantee that patients will receive personal benefit from taking part in this study. However, by taking part in this study, patients may benefit if the treatment turns out to be effective. Furthermore, patients will have close medical monitoring of their health condition by blood tests and other tests

during clinic visits.

Contacts

Public
Quintiles

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Scientific
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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

* Men and women, aged 18 or older.;* Histologically or cytologically confirmed cholangiocarcinoma. Subjects will be assigned to 1 of 3 cohorts:;a. Cohort A: FGFR2 translocations.;b. Cohort B: other FGF/FGFR alterations.;c. Cohort C (US only): negative for FGF/FGFR alterations.;* Radiographically measurable disease per RECIST v1.1.;* Documentation of FGF/FGFR gene alteration status.;* Documented disease progression after at least 1 line of prior systemic therapy.;* ECOG performance status of 0 to 2.;* Life expectancy * 12 weeks.

Exclusion criteria

* Prior receipt of a selective FGFR inhibitor.;* History of and/or current evidence of ectopic mineralization/calcification, including but not limited to soft tissue, kidneys, intestine, myocardia, or lung, excepting calcified lymph nodes and asymptomatic arterial or cartilage/tendon calcifications.;* Current evidence of clinically significant corneal or retinal disorder confirmed by ophthalmologic examination.;* Use of any potent CYP3A4 inhibitors or inducers within 14 days or 5 half-lives, whichever is shorter, before the first dose of study drug.

Study design

Design

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

Recruitment

NL

Recruitment status:	Will not start
Enrollment:	4
Type:	Anticipated

Medical products/devices used

Product type:	Medicine
Brand name:	INCB054828
Generic name:	Unknown

Ethics review

Approved WMO

Date:	30-06-2017

Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Not approved Date:	14-11-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

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	EUCTR2016-002422-36-NL
ClinicalTrials.gov	NCT02924376
CCMO	NL62044.100.17