INCB 54828-201
A Phase 2, Open-Label, Single-Agent, Multicenter Study to Evaluate the Efficacy and Safety of INCB054828 in Subjects With Metastatic or Surgically Unresectable Urothelial Carcinoma Harboring FGF/FGFR Alterations (FIGHT-201)

Published: 29-11-2016
Last updated: 12-04-2024

The primary objective of this study is to evaluate the objective response rate (ORR) of INCB054828 as a monotherapy in the treatment of metastatic or surgically unresectable urothelial carcinoma harboring FGF/FGFR 3 mutations or fusions. The...

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Renal and urinary tract neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON49349

Source
ToetsingOnline

Brief title
INCB 54828201

Condition

- Renal and urinary tract neoplasms malignant and unspecified

Synonym
bladder cancer, urothelial carcinoma

Research involving
Human

Sponsors and support

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

Intervention

Keyword: FGF/FGFR, INCB054828, phase 2, urothelial carcinoma

Outcome measures

Primary outcome

Objective response rate in subjects with FGFR3 mutations or fusions based on central genomics laboratory results and INCB054828 administered using a continuous dose regimen (Cohort A-CD). Response will be based on review of scans by a centralized radiological review committee.

Secondary outcome

The secondary endpoints of this study include:

* Objective response rate in all subjects with FGFR3 mutations or fusions based on central genomics laboratory results and using an intermittent dose regimen (Cohort A-ID). Response will be based on review of scans by a centralized radiological review committee.
* Objective response rate in subjects with FGFR3 mutations or fusions based on central genomics laboratory results and using a continuous dose regimen (Cohort A-CD) and intermittent dose regimen (Cohort A-ID).

Response will be based on review of scans by centralized radiological review committee.

* Objective response rate in all subjects receiving INCB054828 administered as continuous dose regimen or intermittent dose regimen (Cohorts A-ID, A-CD, and B combined). Response will be based on review of scans by a centralized radiological review committee.

* Objective response rate in subjects with all other FGF/FGFR alterations (Cohort B). Response will be based on review of scans by a centralized radiological review committee.

* Progression-free survival (Cohort A-ID, Cohort A-CD, and Cohort B, separately).

* Duration of response (Cohort A-ID, Cohort A-CD, and Cohort B, separately).

* Overall survival (Cohort A-ID, Cohort A-CD, and Cohort B, separately).

* Safety and tolerability, assessed by monitoring the frequency, duration, and severity of adverse events (AEs); through physical examinations; by evaluating changes in vital signs and electrocardiograms (ECGs); and through clinical laboratory blood and urine sample evaluations.

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, including urothelial 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/nonresectable or metastatic urothelial carcinoma with fibroblast growth factor (FGF)/FGFR genetic alterations.

Study objective

The primary objective of this study is to evaluate the objective response rate (ORR) of INCB054828 as a monotherapy in the treatment of metastatic or surgically unresectable urothelial carcinoma harboring FGF/FGFR 3 mutations or fusions.

The secondary objectives of this study are to

- To evaluate the efficacy of INCB054828 in subjects with advanced/metastatic or surgically unresectable urothelial cancer with
different molecular subgroups.
- evaluate the safety and tolerability of INCB054828 and
- evaluate other clinical efficacy measurements, including duration of response (DOR), progression free survival (PFS), and overall survival (OS).

An exploratory objective of this study is to obtain additional data on predictive biomarkers to identify subgroups that would benefit most from INCB054828 in the presence of FGF/FGFR alterations.

Study design

This is an open-label monotherapy study of INCB054828. Subjects will be enrolled into 1 of 3 cohorts. A subject*s cohort will be determined by FGF/FGFR gene alteration status.
* Cohort A-ID: FGFR3 mutations or fusions (n = 100); this cohort will complete enrollment before Cohort A-CD begins enrolling subjects.
* Cohort A-CD: FGFR3 mutations or fusions (n = 100)

* Cohort B: all other FGF/FGFR alterations (40 subjects)

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),14 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.

Subjects will be tested on hepatitis B and C 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.

Patients may be withdrawn from participation if FGF/FGFR alteration is not confirmed by the central lab and the patient does not benefit from treatment.

Contacts

Public
Incyte Corporation

Augustine Cut-Off 1801
Wilmington DE 19803
US
Scientific
Incyte Corporation

Augustine Cut-Off 1801
Wilmington DE 19803
US

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. For subjects in Japan, if the subject is below the age of 20 years, voluntary agreement shall be obtained from the subject and the representative or legal guardian using the written consent form., * Histologically documented metastatic or surgically unresectable urothelial carcinoma; may include primary site from urethra, ureters, upper tract, renal pelvis, and bladder., * Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1, or 2.
* Life expectancy * 12 weeks. , * Radiographically measurable disease per RECIST v1.1., * Documented FGF/FGFR alteration and have either:
* have failed at least 1 previous treatment for their metastatic or surgically unresectable urothelial carcinoma (ie, chemotherapy, immunotherapy), or
* have not received chemotherapy for metastatic or surgically unresectable urothelial carcinoma due to poor performance status (ie,
ECOG performance status of 2) and insufficient renal function (ie, creatinine clearance < 60 mL/min or local guidelines)., * Willingness to avoid pregnancy or fathering children. For subjects in Japan, female subjects who have been amenorrhoeic for at least 12 months resulting from chemotherapy/radiotherapy are considered of childbearing potential and should agree to use adequate contraceptive measures.

Exclusion criteria

* Treatment with other investigational study drug for any indication for any

reason, or receipt of anticancer medications within 28 days before first dose of study drug. Subjects must have recovered (Grade * 1 or at pretreatment baseline) from AEs from previously administered therapies.
* Prior receipt of a selective FGFR inhibitor.
* Abnormal laboratory parameters:
* Total bilirubin * 1.5 × upper limit of normal (ULN; * 2.5 × ULN if Gilbert syndrome or metastatic disease involving liver).
* Aspartate aminotransferase (AST) and alanine aminotransferase (ALT) > 2.5 × ULN (AST and ALT > 5 × ULN in the presence of liver metastases).
* Creatinine clearance * 30 mL/min based on Cockroft-Gault.
* Serum phosphate > institutional ULN.
* Serum calcium outside of the institutional normal range or serum albumin-corrected calcium outside of the institutional normal range when serum albumin is outside of the institutional normal range., * 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., * Known hypersensitivity or severe reaction to INCB054828 or excipients of INCB054828 study drug., * Inability or unwillingness to swallow INCB054828 or significant gastrointestinal disorder(s) that could interfere with the absorption, metabolism, or excretion of INCB054828., * Subjects who require hemodialysis.

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):	12-01-2017
Enrollment:	7
Type:	Actual

Medical products/devices used

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

Ethics review

Approved WMO Date:	29-11-2016
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	28-04-2017
Application type:	First submission
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	08-06-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	24-07-2017
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	20-02-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-04-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)

Approved WMO Date:	06-06-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	10-07-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	05-09-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	01-11-2018
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	25-03-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	03-04-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	22-05-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	19-06-2019
Application type:	Amendment

Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	06-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-11-2019
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	13-07-2020
Application type:	Amendment
Review commission:	MEC-U: Medical Research Ethics Committees United (Nieuwegein)
Approved WMO Date:	14-07-2020
Application type:	Amendment
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	EUCTR2016-001321-14-NL
ClinicalTrials.gov	NCT02872714
CCMO	NL59441.100.16