FIDES-01

Derazantinib in Subjects With FGFR2 Gene Fusion-, Mutation- or Amplification- Positive Inoperable or Advanced Intrahepatic Cholangiocarcinoma

NCT-Nummer:
NCT03230318

Studienbeginn:
November 2017

Letztes Update:
01.02.2021

Wirkstoff:
Derazantinib
Indikation (Clinical Trials):
Cholangiocarcinoma, Carcinoma, Hepatocellular

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 2

Sponsor:
Basilea Pharmaceutica

Collaborator:
-

Studien-Informationen

Brief Summary:

This pivotal, open-label, single-arm study will evaluate the anti-cancer activity of

derazantinib by Objective Response Rate (ORR) by central radiology review as per RECIST v1.1

in subjects with inoperable or advanced intrahepatic cholangiocarcinoma (iCCA) whose tumors harbor FGFR2 gene fusions (by FISH performed by the central laboratory) or FGFR2 gene mutations or amplifications (based on NGS testing performed or commissioned by the respective study center) and who received at least one prior regimen of systemic therapy. Subjects will be dosed orally once per day at 300 mg of derazantinib capsules.

Ein-/Ausschlusskriterien

Inclusion Criteria:

1. Signed written informed consent granted prior to initiation of any study-specific procedures

2. 18 years of age or older

3. Histologically or cytologically confirmed locally advanced, inoperable (where surgery is not indicated due to disease extension, co-morbidities, or other technical reasons), or metastatic iCCA or mixed histology tumors (combined hepatocellular-cholangiocarcinoma [cHCC-CCA])

4. Substudy 1: FGFR2 gene fusion status based on the following assessments:

a) If central laboratory designated by Sponsor: Positive FISH test; and/or b) If non-central laboratory: i) Positive FISH or NGS test: patients may be enrolled and may start dosing, but central confirmation is required* ii) Negative FISH or NGS test: tissue may be submitted to the central laboratory designated by the Sponsor, and patients may only be enrolled if the central test is positive

*Using standard protocols and approved by local IRB/EC, by CLIA or other similar agency.

Substudy 2: FGFR2 mutation/amplification status based on local NGS testing performed or commissioned by the respective study site.

5. Received at least one regimen of prior systemic therapy and then experienced

documented radiographic progression

6. Measurable disease by RECIST version 1.1 criteria

7. ECOG performance status ≤ 1

8. Adequate organ functions as indicated by the following laboratory values (based on screening visit values from the central laboratory).

- Hematological

- Hemoglobin (Hgb) ≥ 9.0 g/dL

- Absolute neutrophil count (ANC) ≥ 1.5 x 10^9/L

- Platelet count ≥ 75 x 109/L

- International normalized ratio (INR) 0.8 to upper limit of normal (ULN) or ≤ 3 for subjects receiving anticoagulant therapy such as Coumadin or heparin

- Hepatic

- Total bilirubin ≤ 2 x ULN

- AST and ALT ≤ 3 ULN (≤ 5 x ULN for subjects with liver metastases)

- Albumin ≥ 2.8 g/dL

- Renal

- Serum creatinine ≤ 1.5 x ULN

- Creatinine clearance of ≥ 30 mL/min as estimated by the Cockcroft-Gault equation

9. Female and male patients of child-producing potential must agree to avoid becoming pregnant or impregnating a partner, respectively, use double-barrier contraceptive measures, oral contraception, or avoidance of intercourse, during the study*, and until at least 120 for 90 days after the last dose of derazantinib.

*From the day of first study medication, or for oral contraception from 14 days before first study medication.

Male patients are considered not to be of child-producing potential if they have azoospermia (whether due to vasectomy or an underlying medical condition). Female

patients are considered not to be of child-producing potential if they are:

- postmenopausal* , or

- have had a hysterectomy and/or bilateral oophorectomy, bilateral salpingectomy or bilateral tubal ligation/occlusion, at least 6 weeks prior to screening, or

- have a congenital or acquired condition that prevents childbearing.

Male or female patients of child-producing potential must agree to comply with one of the following until at least 120 days after the last dose of derazantinib:

1. Abstinence from heterosexual activity**

2. Using (or having their partner use) an acceptable method of contraception during heterosexual activity. Acceptable methods of contraception are***:

- any ONE of:

- an intrauterine device (IUD)

- vasectomy of a female patient's male partner

- a contraceptive rod implanted into the skin.

- any TWO in combination of:

- diaphragm with spermicide (cannot be used in conjunction with cervical cap/spermicide)

- cervical cap with spermicide (nulliparous women only)

- contraceptive sponge (nulliparous women only)

- male condom or female condom (cannot be used together)

- hormonal contraceptive (oral contraceptive pill [estrogen/progestin pill or progestin-only pill], contraceptive skin patch, vaginal contraceptive ring, or subcutaneous contraceptive injection)

*Postmenopausal is defined as at least 12 months with no menses without an alternative medical cause; in women < 45 years of age a high follicle stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a post -menopausal state in women not using hormonal contraception

or hormonal replacement therapy. In the absence of 12 months of amenorrhea, a single FSH measurement is not sufficient.

- Abstinence (relative to heterosexual activity) can be used as the sole method of contraception if it is consistently employed as the subject's preferred and usual lifestyle and if considered acceptable by local regulatory agencies and ERCs/IRBs. Periodic abstinence (e.g., calendar, ovulation, sympto-thermal, post-ovulation methods, etc.) and withdrawal are not acceptable methods of contraception.
- If a contraceptive method listed above is restricted by local regulations/guidelines, then it does not qualify as an acceptable method of contraception for subjects participating at sites in this country/region.

Exclusion Criteria:

1. Receipt of treatment before the first dose of study drug (Cycle 1 Day 1) within an interval shorter than the following, as applicable:
- One chemotherapy or biological (e.g., antibody) cycle interval
- Five half-lives of any small-molecule investigational or licensed medicinal product
- Two weeks, for any investigational medicinal product with an unknown half-life
- Four weeks of curative radiotherapy
- Seven days of palliative radiotherapy
- 28 days of radiotherapy

2. Major surgery, locoregional therapy, or radiation therapy within four weeks of the first dose of derazantinib

3. Previous treatment with any FGFR inhibitor (e.g., Balversa® [erdafitinib], Pemazyre® [pemigatinib], infigratinib, rogaratinib, futibatinib, lenvatinib, ponatinib, dovitinib, nintedanib, AZD4547, LY2784455).

- Subjects who received less than four weeks of therapy and were unable to continue therapy due to toxicity will be allowed to participate

4. Unable or unwilling to swallow the complete daily dose of derazantinib capsules

5. Clinically unstable central nervous system (CNS) metastases (to be eligible, subjects must have stable disease ≥ 3 months, confirmed by magnetic resonance imaging (MRI) or computed tomography (CT) scan, and/or have CNS metastases well controlled by low-dose steroids, anti-epileptics, or other symptom-relieving medications)

6. Current evidence of clinically significant corneal or retinal disorder likely to increase the risk of eye toxicity, including but not limited to bullous/band keratopathy, keratoconjunctivitis (unless keratoconjunctivitis sicca), corneal abrasion, inflammation/ulceration, confirmed by ophthalmologic examination.

7. Concurrent uncontrolled or active hepatobiliary disorders, untreated or ongoing complications after laparoscopic procedures or stent placement, including but not limited to active cholangitis, biloma or abscess (to be eligible, the subjects have to be treated and disorders/complications should be resolved within 2 weeks prior to the first dose of derazantinib)

8. History of significant cardiac disorders:

- Myocardial infarction (MI) or congestive heart failure defined as Class II to IV per the New York Heart Association (NYHA) classification within 6 months of the first dose of derazantinib (MI that occurred > 6 months prior to the first dose of derazantinib will be permitted)

- QTcF >450 msec (males or females)

9. Serum electrolyte abnormalities defined as follows:

- Hyperphosphataemia: Serum phosphate > institutional ULN

- Hyperkalemia: > 6.0 mmol/L

- Hypokalemia: < 3.0 mmol/L

- Hypercalcemia: corrected serum calcium < 1.75 mmol/L (< 7.0 mg/dL)

- Hypocalcemia: corrected serum calcium > 3.1 mmol/L (> 12.5 mg/dL)

- Hypomagnesemia: < 0.4 mmol/L (< 0.9 mg/dL)

10. Significant gastrointestinal disorder(s) that could, in the opinion of the Investigator, interfere with the absorption, metabolism, or excretion of derazantinib (e.g., Crohn's disease, ulcerative colitis, extensive gastric resection)

11. History of additional malignancy that is progressing or requires active treatment. Exceptions include basal cell carcinoma of the skin, squamous cell carcinoma of the skin that has undergone potentially curative therapy, and in situ cervical cancer.

12. Concurrent uncontrolled illness not related to cancer, including but not limited to:

- Psychiatric illness/substance abuse/social situation that would limit compliance with study requirements

- Known uncontrolled human immunodeficiency virus (HIV) infection

- Severe bacterial, fungal, viral and/or parasitic infections on therapeutic oral or IV medication at the time of first dose of study drug administration

13. Blood or albumin transfusion within 5 days of the blood draw being used to confirm eligibility

14. Pregnant or breast feeding

15. Known hypsersensitivity to derazantinib, or to any of the study drug excipients (starch, lactose, crospovidone, magnesium stearate)

Studien-Rationale

Primary outcome:

1. Substudy 1: Anti-cancer activity of derazantinib by Objective Response Rate (ORR) (Time Frame - Up to approximately 32 weeks):
ORR will be assessed by central radiology review as per RECIST version 1.1

2. Substudy 2: Anti-tumor activity of derazantinib by Progression Fress Survival at 3 months (PFS 3) (Time Frame - 3 months):
PFS 3 will be assessed based on survival status or central radiology review (Response Evaluation Criteria in Solid Tumors, RECIST 1.1)

Secondary outcome:

1. Safety of derazantinib as assessed by adverse events (Time Frame - Up to approximately 36 weeks):
Adverse events will be graded using NCI CTCAE guidelines, version 4.03

2. Anti-cancer activity of derazantinib by duration of response (DoR) (Time Frame - Up to approximately 32 weeks):
DoR will be assessed by central radiology review per RECIST version 1.1

3. Anti-cancer activity of derazantinib by progression free survival (PFS) (Time Frame - Up to approximately 32 weeks):
PFS will be assessed by central radiology review per RECIST version 1.1

4. Anti-cancer activity of derazantinib by overall survival (OS) (Time Frame - Up to approximately 36 weeks):
OS will be calculated from the first date of receiving study drug until death

5. Health-related quality of life as assessed by the European Organisation for Research and Treatment of Cancer (EORTC) QLQ-C30 questionnaire (Time Frame - Up to approximately 36 weeks)

6. Health-related quality of life as assessed by the EORTC QLQ-BIL21 questionnaire (Time Frame - Up to approximately 36 weeks)

7. Health-related quality of life as assessed by the EuroQol EQ-5D questionnaire (Time Frame - Up to approximately 36 weeks)

8. Substudy 2: Anti-cancer activity of derazantinib by Objective Response Rate (Time Frame - Up to approximately 32 weeks):
ORR will be assessed by central radiology review as per RECIST version 1.1

Geprüfte Regime

- derazantinib:
  derazantinib will be orally administered at 300 mg once per day one hour prior to or two hours after a meal and is supplied as 100 mg capsules.

Studienleiter

Stephan Braun, MD
Study Director
Basilea Pharmaceutica

Kontakt

Stephan Braun, MD

Kontakt:
Phone: +41 61 606 12 25
E-Mail: stephan.braun@basilea.com

Frédérique Cantero, MD
Kontakt:
Phone: +41 61 606 1329
E-Mail: frederique.cantero@basilea.com

Studienlocations (3 von 40)

Mayo Clinic
85054 Phoenix
United States

Status: Rekrutierend

Mayo Clinic
32224 Jacksonville
United States

Status: Rekrutierend

Moffitt Cancer Center
33612-9416 Tampa
United States

Status: Noch nicht rekrutierend

Winship Cancer Institute of Emory University
30322 Atlanta
United States

Status: Rekrutierend

Mayo Clinic
55905 Rochester
United States

Status: Rekrutierend

Memorial Sloan Kettering Cancer Center - Sidney Kimmel Center for Prostate and Urologic Cancers

10065-6800 New York
United States

Status: Rekrutierend

Abramson Cancer Center of the University of Pennsylvania
19104 Philadelphia
United States

Status: Rekrutierend

Vanderbilt-Ingram Cancer Center
37232 Nashville
United States

Status: Rekrutierend

The University of Texas Southwestern Medical Center
75390 Dallas
United States

Status: Rekrutierend

University of Texas MD Anderson Cancer Center
77030 Houston
United States

Status: Rekrutierend

University of Washington Medical Center
98109 Seattle
United States

Status: Rekrutierend

Hôpital Erasme
1070 Brussels
Belgium

Status: Rekrutierend

Cliniques Universitaires Saint-Luc
1200 Brussels

Belgium

Status: Rekrutierend

Antwerp University Hospital
2650 Edegem
Belgium

Status: Rekrutierend

Tom Baker Cancer Centre
T2N 4N2 Calgary
Canada

Status: Rekrutierend

Princess Margaret Cancer Centre
M5G 2M9 Toronto
Canada

Status: Rekrutierend

CHU Grenoble Alpes
38700 La Tronche
France

Status: Rekrutierend

Gustave Roussy
94805 Villejuif
France

Status: Rekrutierend

Universitätsklinikum Frankfurt
60590 Frankfurt am Main
(Hessen)
Germany

Status: Rekrutierend

Universitätsklinikum Hamburg-Eppendorf (UKE)
20246 Hamburg

(Hamburg)
Germany

Status: Rekrutierend

Medizinische Hochschule Hannover (MHH)
30625 Hannover
(Niedersachsen)
Germany

Status: Noch nicht rekrutierend

Universitäts-Brustzentrum am Universitätsklinikum des Saarlandes
Kirrberger Straße 100
66424 Homburg
Deutschland

Status: Rekrutierend

Universitätsmedizin der Johannes Gutenberg-Universität Mainz
55131 Mainz
(Rheinland-Pfalz)
Germany

Status: Rekrutierend

St. James's Hospital
D08 NHY1 Dublin
Ireland

Status: Rekrutierend

Sant'Orsola-Malpighi Hospital, University of Bologna
40138 Bologna
Italy

Status: Rekrutierend

Fondazione IRCCS Istituto Nazionale dei Tumori
20133 Milan
Italy

Status: Rekrutierend

Ospedale San Gerardo
20900 Monza
Italy

Status: Rekrutierend

Istituto Oncologico Veneto - IRCCS
35128 Padova
Italy

Status: Rekrutierend

Azienda Ospedaliero-Universitaria Pisana
56126 Pisa
Italy

Status: Rekrutierend

Humanitas Cancer Center, Istituto Clinico Humanitas IRCCS
20089 Rozzano
Italy

Status: Rekrutierend

Seoul National University Hospital
3080 Seoul
Korea, Republic of

Status: Rekrutierend

Samsung Medical Center
6351 Seoul
Korea, Republic of

Status: Rekrutierend

The Catholic University of Korea, Seoul St. Mary's Hospital
6591 Seoul
Korea, Republic of

Status: Rekrutierend

Vall d'Hebrón University Hospital

08035 Barcelona
Spain

Status: Rekrutierend

Hospital General Universitario Gregorio Marañón
28007 Madrid
Spain

Status: Rekrutierend

Hospital Universitario 12 de Octubre
28041 Madrid
Spain

Status: Rekrutierend

Universitätsspital Basel
4031 Basel
Switzerland

Status: Rekrutierend

University College London Hospitals NHS Foundation Trust
NW1 2BU Euston
United Kingdom

Status: Rekrutierend

Beatson West of Scotland Cancer Centre
G120YN Glasgow
United Kingdom

Status: Rekrutierend

The Royal Marsden
SM2 5PT Sutton
United Kingdom

Status: Rekrutierend

Quelle: ClinicalTrials.gov