A Phase II, Non-randomized, Single Arm, Translational Study of Cabozantinib for Patients With Hepatocellular Carcinoma (HCC) Refractory to Lenvatinib Treatment

NCT-Nummer:
NCT04511455

Studienbeginn:
Dezember 2020

Letztes Update:
24.12.2020

Wirkstoff:
Cabozantinib
Indikation (Clinical Trials):
Carcinoma, Carcinoma, Hepatocellular

Geschlecht:
Alle

Altersgruppe:
Erwachsene (18+)

Phase:
Phase 2

Sponsor:
Institut für Klinische Krebsforschung IKF GmbH at Krankenhaus Nordwest

Collaborator:
Ipsen

Studien-Informationen

Detailed Description:

This is a open-label, single-arm, multicenter phase II trial for patients with locally advanced and/or metastatic and/or unresectable hepatocellular carcinoma (HCC).

Patients who have histologically proven or were clinically diagnosed (by guideline criteria

in cirrhotic patients) with locally advanced or metastatic and/or unresectable HCC will be included to receive cabozantinib peroral 60 mg/day. A stepwise dose de-escalation schedule on individual level is available for patients with lower tolerability against cabozantinib.

The study treatment will be limited to a maximum of 12 months (including temporary interruptions).

Tumor tissue will be collected for accompanying research project. (Participation is optional for participant).

During treatment, clinical visits (blood cell counts, ECG, detection of toxicity) occur every four weeks during treatment phase. Safety will be monitored continuously by careful monitoring of all adverse events (AEs) and serious adverse events (SAEs) reported.

During treatment, tumor response will be assessed by the Investigator according to RECIST 1.1 (radiological imaging by CT and/or MRI of the chest, abdomen, pelvis and all other sites of disease every 10 weeks until end of treatment (EOT) and every 12 weeks during follow-up (FU), in case of EOT due to other reasons than progressive disease. Safety-FU visit and Survival FU visits will be assessed 30 days-, and every 12 weeks after EOT.

Ein-/Ausschlusskriterien

Inclusion Criteria:

1. Fully-informed written consent.

2. Males and females ≥ 18 years of age.

*There are no data that indicate special gender distribution. Therefore, patients will be enrolled in the study gender-independently.

3. Locally advanced or metastatic and/or unresectable HCC with diagnosis confirmed by histology/ cytology or clinically by guideline criteria in cirrhotic patients

4. Disease that is not amenable to curative surgical and/or locoregional therapies, or progressive disease after surgical and /or locoregional therapies.

5. Patients who have shown progressive disease despite of lenvatinib treatment (in terms of lenvatinib monotherapy or combination therapy with IO) OR patients must have had their treatment interrupted after at least 1 administration, as treatment with lenvatinib is no longer clinically indicated due to the level of toxicities.

6. ECOG performance status ≤ 2.

7. Resolution of any acute, clinically significant treatment-related toxicity from prior therapy to Grade 1 prior to study entry, with the exception of alopecia.

8. For women of childbearing potential and men who are sexually active with women of childbearing potential: agreement to remain abstinent (refrain from heterosexual intercourse) or use contraceptive methods.

Exclusion Criteria:

1. Unwillingness to give informed consent for participation in the study.

2. Prior sorafenib treatment.

3. Pregnancy or breastfeeding, or intention of becoming pregnant during study treatment or within at least 5 months after last dose of study treatment.

4. Women of childbearing potential must have a negative serum pregnancy test result within 14 days prior to initiation of study treatment.

5. Significant portal hypertension (moderate or severe ascites).

6. Known fibrolamellar HCC, sarcomatoid HCC, or mixed cholangiocarcinoma and HCC.

7. Liver cirrhosis Child-Pugh B (> 7 points).

8. Severely impaired kidney function.

9. History of encephalopathy in past 12 months.

10. Significant cardiovascular disease (such as New York Heart Association Class II or greater cardiac disease, myocardial infarction, or cerebrovascular accident) within 3 months prior to initiation of study treatment, unstable arrhythmia, or unstable angina.

11. Baseline QTcF >500 ms.

12. Major surgical procedure, other than for diagnosis, within 4 weeks prior to initiation of study treatment, or anticipation of need for a major surgical procedure during the study.

13. Severe infection within 4 weeks prior to initiation of study treatment, including, but not limited to, hospitalization for complications of infection, bacteremia, or severe pneumonia.

14. Any other disease, metabolic dysfunction, physical examination finding, or clinical laboratory finding that contraindicates the use of an investigational drug, may affect the interpretation of the results, or may render the patient at high risk from treatment complications.

15. Elevations of AST/ALT exceeding 5 X ULN.

16. Treatment with investigational systemic therapy within 28 days prior to initiation of study treatment.

17. Prior cabozantinib use.

18. Is currently participating or has participated in a study of an investigational agent or has used an investigational device within 4 weeks prior to the first dose of study treatment.

19. Patients who have been incarcerated or involuntarily institutionalized by court order or by the authorities § 40 Abs. 1 S. 3 Nr. 4 AMG.

20. Patients who are unable to consent because they do not understand the nature, significance and implications of the clinical trial and therefore cannot form a rational intention in the light of the facts [§ 40 Abs. 1 S. 3 Nr. 3a AMG].

Studien-Rationale

Primary outcome:

1. Time-on-treatment (Time Frame - at study end (approx. 30 months after FPI)):
Time on treatment will be assessed as time from date of first dose of cabozantinib intake till date

of permanent discontinuation of treatment.

Secondary outcome:

1. Overall survival (OS) (Time Frame - at 18 months after last patient randomized):
Survival rates will be assessed from the date of first dose of cabozantinib intake to the date of death from any cause using Kaplan-Meier methods.

2. Progression free survival (PFS) (Time Frame - at study end (approx. 18 months after last patient randomized)):
Survival rates for the different time points will be determined using the Kaplan-Meier analysis and RECIST 1.1.

3. Objective response rate (ORR) (Time Frame - at study end (approx. 18 months after last patient randomized)):
Objective response rate will be defined as the proportion of subjects experiencing a confirmed complete response (CR) or confirmed partial response (PR) per RECIST 1.1.

4. Duration of response (Time Frame - at study end (approx. 18 months after last patient randomized)):
Time from documentation of tumor response to disease progression.

5. Treatment exposure (Time Frame - at study end (approx. 18 months after last patient randomized)):
Time on treatment/dose intensity/dose reductions

6. Toxicity: o Treatment-related adverse events (TRAEs) o TRAE related treatment interruptions o TRAE related treatment modifications o TRAE related treatment discontinuations (Time Frame - at study end (approx. 18 months after last patient randomized)):
All observed toxicities and side effects will be graded according to NCI CTCAE v5.0 and the degree of association of each with the study treatment assessed and summarized.

7. Change in ECOG Performance Status (Time Frame - at study end (approx. 18 months after last patient randomized)):
Eastern Cooperative Oncology Group patient performance status (Grading from 0 to 5)

8. Change in ALBI Grade (Time Frame - at study end (approx. 18 months after last patient randomized)):
ALBI score = -0.085 × (albumin g/L) + 0.66 × l g(TBil µmol/L)

9. Change in Child Pugh Score (Time Frame - at study end (approx. 18 months after last patient randomized)):
Child-Pugh Classification Score (Grading from A to C)

10. Translational research (Time Frame - at study end (approx. 18 months after last patient randomized)):
Correlation of biomarkers potentially associated with clinical efficacy (OS, PFS and ORR) of cabozantinib by NGS Oncopanel analysis and VEGF module expression analysis.

Geprüfte Regime

- Cabozantinib:
  Cabozantinib 60 mg/day peroral

Studienleiter

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Studienlocations (1 von 1)

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Status: Rekrutierend