The purpose of this study is to evaluate the effect of Cabozantinib (XL184) compared with placebo on overall survival in subjects with advanced hepatocellular carcinoma who have received prior sorafenib.

**Condition** | **Intervention** | **Phase**
--- | --- | ---
Hepatocellular Carcinoma | Drug: Cabozantinib (XL184)  
 Drug: Placebo | Phase 3

**Primary Outcome Measures:**
- Overall Survival (OS) [Time Frame: Up to 38 months] [Designated as safety issue: No]
  - OS is defined as the time from randomization to death from any cause.

**Secondary Outcome Measures:**
- Progression-Free Survival (PFS) [Time Frame: Up to 38 months] [Designated as safety issue: No]
Duration of PFS is defined as the time of randomization to the earlier of the following events: progressive disease or death due to any cause.

- Objective Response Rate (ORR) [Time Frame: Up to 38 months] [Designated as safety issue: No]

ORR is measured by radiologic assessment every 8 weeks after randomization until disease progression or discontinuation of study treatment. ORR is the proportion of subjects experiencing a confirmed complete response (CR) or confirmed partial response (PR).

Estimated Enrollment: 760
Study Start Date: August 2013
Estimated Primary Completion Date: October 2016 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Experimental: Cabozantinib (XL184)</td>
<td>Drug: Cabozantinib (XL184)</td>
</tr>
<tr>
<td>Cabozantinib (XL184): oral cabozantinib tablet once a day</td>
<td>Drug: Placebo</td>
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<tr>
<td>Placebo Comparator: Placebo</td>
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<tr>
<td>Oral cabozantinib-matched placebo tablet once daily</td>
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</tbody>
</table>

Eligibility

Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No

Criteria

Select Inclusion Criteria:

1. Histological or cytological diagnosis of HCC.
2. The subject has disease that is not amenable to a curative treatment approach.
3. Received prior sorafenib.
4. Progression following at least 1 prior systemic treatment for HCC.
5. Recovery to from toxicities related to any prior treatments.
6. ECOG performance status of 0 or 1.
7. Adequate hematologic and renal function, based upon meeting protocol defined laboratory criteria within 7 days before randomization.
8. Child-Pugh Score of A.
9. Antiviral therapy per local standard of care if active hepatitis B (HBV) infection.
10. Sexually active fertile subjects (male and female) must agree to use medically accepted methods of contraception during the course of the study and for 4 months after the last dose of study treatment.
11. Female subjects of childbearing potential must not be pregnant at screening.

Select Exclusion Criteria:

1. Fibrolamellar carcinoma or mixed hepatocellular cholangiocarcinoma.
2. Receipt of more than 2 prior systemic therapies for advanced HCC.
3. Any type of anticancer agent (including investigational) within 2 weeks before randomization.
4. Radiation therapy within 4 weeks (2 weeks for radiation for bone metastases) or radionuclide treatment within 6 weeks of randomization.
6. Known brain metastases or cranial epidural disease unless adequately treated with radiotherapy and/or surgery and stable for at least 3 months before randomization.
7. Concomitant anticoagulation, at therapeutic doses, with anticoagulants.
8. Serious illness other than cancer that would preclude safe participation in the study.
9. Subjects with untreated or incompletely treated varices with bleeding or high risk for bleeding.
10. Moderate or severe ascites.
11. Pregnant or lactating females.
12. Diagnosis of another malignancy within 2 years before randomization, except for superficial skin cancers, or localized, low-grade
tumors.

Contacts and Locations

Choosing to participate in a study is an important personal decision. Talk with your doctor and family members or friends about deciding to join a study. To learn more about this study, you or your doctor may contact the study research staff using the Contacts provided below. For general information, see Learn About Clinical Studies.

Please refer to this study by its ClinicalTrials.gov identifier: NCT01908426

Contacts

Contact: Exelixis Clinical Trials 1-888-EXELIXIS (888-393-5494)
Contact: Backup or International 650-837-7400

Show 142 Study Locations

Sponsors and Collaborators
Exelixis

More Information

No publications provided

Responsible Party: Exelixis
ClinicalTrials.gov Identifier: NCT01908426
Other Study ID Numbers: XL184-309
Study First Received: July 23, 2013
Last Updated: October 27, 2014
Health Authority: United States: Food and Drug Administration

Keyw ords provided by Exelixis:
cabozantinib tyrosine kinase inhibitor
XL184 MET
liver cancer vascular endothelial growth factor receptor 2 (VEGFR2)
hepatocellular carcinoma

Additional relevant MeSH terms:
Carcinoma Liver Neoplasms
Carcinoma, Hepatocellular Neoplasms
Adenocarcinoma Neoplasms by Histologic Type
Digestive System Diseases Neoplasms by Site
Digestive System Neoplasms Neoplasms, Glandular and Epithelial
Liver Diseases

ClinicalTrials.gov processed this record on November 16, 2014