Purpose

This clinical study evaluates the efficacy and safety of regorafenib in patients with advanced liver cancer who have progressed on sorafenib treatment.

Approximately 530 patients who meet the entry criteria will be randomly assigned in a 2:1 ratio to regorafenib or placebo (1/3 chance to receive placebo).

Primary endpoint of the study is overall survival.

<table>
<thead>
<tr>
<th>Condition</th>
<th>Intervention</th>
<th>Phase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carcinoma, Hepatocellular</td>
<td>Drug: Regorafenib (BAY73-4506)</td>
<td>Phase 3</td>
</tr>
<tr>
<td></td>
<td>Drug: Placebo</td>
<td></td>
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</tbody>
</table>

Resource links provided by NLM:

- MedlinePlus related topics: Cancer
- Drug Information available for: Sorafenib, Sorafenib tosylate, Regorafenib
- Genetic and Rare Diseases Information Center resources: Liver Cancer

Further study details as provided by Bayer:

Primary Outcome Measures:
- Overall survival [ Time Frame: Approximately 33 months ] [ Designated as safety issue: No ]

Secondary Outcome Measures:
- Time to progression [ Time Frame: Approximately 33 months ] [ Designated as safety issue: No ]
- Progression free survival (PFS) [ Time Frame: Approximately 33 months ] [ Designated as safety issue: No ]
- Objective tumor response [ Time Frame: Approximately 33 months ] [ Designated as safety issue: No ]
- Disease control [ Time Frame: Approximately 33 months ] [ Designated as safety issue: No ]

Estimated Enrollment: 530
Study Start Date: May 2013
Estimated Study Completion Date: October 2016
Estimated Primary Completion Date: October 2015 (Final data collection date for primary outcome measure)

<table>
<thead>
<tr>
<th>Arms</th>
<th>Assigned Interventions</th>
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</table>
| **Experimental:** Regorafenib  
160 mg orally (p.o.) every day (qd) for 3 weeks of every 4 week cycle (i.e. 3 weeks on, 1 week off) plus BSC (Best Supportive Care) | Drug: Regorafenib (BAY73-4506)  
Regorafenib, 40 mg tablets |
| **Placebo Comparator:** Placebo  
4 matching placebo tablets for 3 weeks of every 4 week cycle (i.e. 3 weeks on, 1 week off) plus BSC | Drug: Placebo  
Placebo tablets matching in appearance |

**Eligibility**

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

**Criteria**

*Inclusion Criteria:*

- Histological or cytological confirmation of HCC (hepatocellular carcinoma) or non-invasive diagnosis of HCC as per American Association for the Study of Liver Diseases criteria in patients with a confirmed diagnosis of cirrhosis
- Barcelona Clinic Liver Cancer stage Category B or C that cannot benefit from treatments of established efficacy with higher priority such as resection, liver transplantation, local ablation, chemoembolization or systemic sorafenib.
- Failure to prior treatment with sorafenib (defined as documented radiological progression according to the radiology charter). Randomization needs to be performed within 8 weeks after the last treatment with sorafenib.
- Tolerability of prior treatment with sorafenib defined as not less than 20 days at a minimum daily dose of 400 mg QD within the last 28 days prior to withdrawal.
- Liver function status Child-Pugh Class A. Child Pugh status should be calculated based on clinical findings and laboratory results during the screening period.
- Local or loco-regional therapy (e.g. surgery, radiation therapy, hepatic arterial embolization, chemoembolization, radiofrequency ablation, percutaneous ethanol injection, or cryoablation) must have been completed >/= 4 weeks before first dose of study medication.
- Eastern Cooperative Oncology Group Performance Status of 0 or 1.
- Adequate bone marrow, liver and renal function as assessed by the following laboratory tests conducted within 7 days before randomization.
- Glomerular filtration rate >/= 30 ml/min/1.73 m² according to the Modification of diet in renal disease abbreviated formula.
- At least one uni-dimensional measurable lesion by computed tomography (CT) scan or magnetic resonance imaging (MRI) according to RECIST (RECIST version 1.1), and modified RECIST for HCC. Tumor lesions situated in a previously irradiated area, or in an area subjected to other loco-regional therapy, may be considered measurable if there has been demonstrated progression in the lesion.
- Life expectancy of at least 3 months.
- Women of childbearing potential and men must agree to use adequate contraception .

*Exclusion Criteria:*

- Sorafenib treatment within 2 weeks of randomization.
- Prior systemic treatment for HCC, except sorafenib.
- Permanent discontinuation of prior sorafenib therapy due to sorafenib related toxicity.
- Known history or symptomatic metastatic brain or meningeal tumors (head CT or MRI at screening to confirm the absence of central nervous system [CNS] disease if patient has symptoms suggestive or consistent with CNS disease).
- Uncontrolled hypertension (systolic blood pressure [BP] > 150 mmHg or diastolic pressure > 90 mmHg despite optimal medical management).
- Uncontrolled ascites (defined as not easily controlled with diuretic or paracentesis treatment).
- Ongoing infection > Grade 2 according to NCI-CTCAE (National Cancer Institute - Common Terminology Criteria for Adverse Events) v. 4.0.
- Hepatitis B is allowed if no active replication is present. Hepatitis C is allowed if no antiviral treatment is required.
- Clinically significant bleeding NCI-CTCAE version 4.0 Grade 3 or higher within 30 days before randomization.
- Arterial or venous thrombotic or embolic events such as cerebrovascular accident (including transient ischemic attacks), deep vein thrombosis or pulmonary embolism within 6 months before the start of study medication.
- Patients unable to swallow oral medications.
- Interstitial lung disease with ongoing signs and symptoms at the time of screening.

**Contacts and Locations**

Please refer to this study by its ClinicalTrials.gov identifier: NCT01774344

**Contacts**

Study of Regorafenib After Sorafenib in Patients With Hepatocellular C...