**Background**

- BTC is a rare and aggressive malignancy arising from the biliary epithelium, characterized by poor prognosis and poor response to current treatments. The 5-year overall survival rate is 5% to 10% for gallbladder cancer and 10% to 40% for cholangiocarcinoma (CCA).
- The incidence of BTC varies widely among different areas of the world. Generally, the incidence of BTC is lower in Europe and North America but higher in Latin America and Asia.
- Like gastric, ovarian, and breast cancer, BTC also involves mutations in members of the ErBB family. Overexpression of EGFR, HER2, HER3, and HER4 range from 23-57%, 4-13%, 12-23%, and 59-60% of BTC, respectively.
- Varlitinib is a potent, orally active inhibitor of the receptor tyrosine kinases of EGFR, HER2, and HER4 with potent anti-tumor effect in preclinical BTC models.
- Varlitinib also showed tumor shrinkage responses and durable disease stabilization in BTC patients in phase I studies.

**About Varlitinib**

**Study Design (continued)**

- **Screening period: 3 weeks**
  - Varlitinib 300 mg BID every day+ Capecitabine 1000 mg/m2 BID for 2 weeks followed by a 1-week rest until disease progression, unacceptable toxicity, consent withdrawal or death
  - Radiological imaging to assess disease status will be performed at baseline and every 6 weeks until disease progression to evaluate the efficacy of treatment according to RECIST Version 1.1
  - Safety follow up: 28 days after the last dose of study medication

**Major Criteria**

- Have historically or cytologically confirmed advanced (unresectable) or metastatic BTC, including intrahepatic or extrahepatic CCA, gallbladder cancer and carcinoma of Ampulla of Vater. This includes clinical diagnosis of BTC with histological confirmation of adenocarcinoma.
- Have received and failed one and only one prior line of systemic treatment for advanced or metastatic disease with radiologic evidence of disease progression. This prior line of systemic treatment must also contain gemcitabine.
- Have not been previously treated with varlitinib or capecitabine as first line therapy for advanced or metastatic disease. For patients who have previously received capecitabine as radioisensitizer or as part of their adjuvant therapy and their disease has relapsed for more than 6 months after their last dose of capecitabine adjuvant therapy, their capecitabine therapy will not be considered as a line of systemic chemotherapy for metastatic/advanced disease, and thus they can participate in the study.
- Have reponded radiologically measurable disease based on Response Evaluation Criteria in Solid Tumors (RECIST) v1.1.
- Have no evidence of biliary duct obstruction, unless obstruction is controlled by local treatment or, in whom the biliary tree can be decompressed by endoscopic or percutaneous stenting with subsequent reduction in bilirubin to below or equal to 1.5 x upper level of normal.
- Have no known metastatic brain lesion(s), including asymptomatic and well controlled lesion(s).

**Statistical Analysis**

The study has not been formally powered for hypothesis testing, however, it has been designed to provide a clear distinction between historical response rates of 6-8% ORR in similar populations treated with capecitabine monotherapy with a 95% confidence interval.

**Study Results**

The enrollment started in December, 2017. As of 3rd September 2018, 46 patient has been screened and 33 patients were enrolled while 3 patients are in screening.

**Baseline Characteristic**

<table>
<thead>
<tr>
<th>Subject by Gender</th>
<th>Male</th>
<th>Female</th>
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<tbody>
<tr>
<td>n=16 (48%)</td>
<td></td>
<td></td>
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<tr>
<td>n=17 (52%)</td>
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**Summary**

- This study is to assess the efficacy of varlitinib plus capecitabine in patients with advanced or metastatic BTC.
- Current varlitinib/capecitabine is safe and tolerated without any unexpected adverse event.
- The study is ongoing and approximately 68 patients will be recruited in the study.

**Other Information**

- **Clinical trial identification:** ClinicalTrials.gov NCT03231176
- Contact information:
  - qinink@csco.org.cn
  - samuel.chi@aslanpharma.com
  - Chi-Hi.Hsieh@aslanpharma.com

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**References**