NRG ONCOLOGY
NRG-GI001
Randomized Phase III Study of Focal Radiation Therapy for Unresectable, Localized Intrahepatic Cholangiocarcinoma

**SCHEMA**

<table>
<thead>
<tr>
<th>REGISTER</th>
<th>Gemcitabine/Cisplatin x 3</th>
<th>Evaluate to confirm no progression:</th>
<th>STRATIFY</th>
<th>Tumor size (≤ 6cm vs. &gt; 6cm)</th>
<th>RAN</th>
<th>DOMIZE</th>
<th>Arm 1: Gem/Cis x 1 -&gt; Liver-directed Radiation Therapy -&gt; Gem/Cis x 4 (Maintenance gemcitabine may be given after completion of Gem/Cis) Vs. Arm 2: Gem/Cis x 5 (Maintenance gemcitabine may be given after completion of Gem/Cis)</th>
</tr>
</thead>
</table>

See [Section 5.0](#) for credentialing requirements, [Section 6.0](#) for radiation therapy details and [Section 7.0](#) for drug therapy details.

**Patient Population:** (See [Section 3.0](#) for Eligibility)

Required Sample Size: 182 patients

Questions that need to be answered at the time of study entry on the OPEN system are available at: [http://www.rlog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=1320](http://www.rlog.org/ClinicalTrials/ProtocolTable/StudyDetails.aspx?study=1320)
NRG G1001/LU207016: RANDOMIZED PHASE III STUDY OF FOCAL RADIATION THERAPY FOR UNRESECTABLE, LOCALIZED INTRAHEPATIC CHOLANGIOCARCINOMA

Eligibility:

1. Pathologically (histologically or cytologically) proven diagnosis of IHC without distant extrahepatic metastasis within 30 days prior to registration.
2. Patient must have 1 lesion with a maximum AXIAL diameter of 12cm. Up to 3 satellite lesions are permitted. Satellite lesions, are defined as lesions less than 2 cm that are within 1 cm of the periphery of the dominant lesion (GTV) are permitted. The satellite lesions are NOT included in the AXIAL diameter measurement. Regional Lymph Node involvement within the porta hepatis (as medial as SMV portal vein confluence) is permitted if nodes are deemed clinically positive (i.e. FDG avid)
3. Appropriate stage for protocol entry, including no distant metastases, based upon the following minimum diagnostic workup:
   - History/physical examination within 30 days prior to registration
   - Assessment by medical oncologist who specializes in treatment of IHC within 30 days prior to registration
4. Pre-randomization Scan (REQUIRED for All Patients): CT scan chest/abdomen/pelvis with multiphasic liver CT scan within 30 days prior to registration. If CT contrast is contraindicated, CT chest without contrast and MRI of abdomen and pelvis is permitted
5. Zubrod Performance Status 0-1 within 30 days prior to registration;
6. Age ≥ 18;
7. CBC/differential obtained within 14 days prior to registration on study, with adequate bone marrow function defined as follows:
   - Absolute neutrophil count (ANC) ≥ 1,500 cells/mm³
   - Platelets ≥ 100,000 cells/mm³; Total bilirubin < 2.5 mg/dl;
   - AST (SGOT) and ALT (SGPT) < 5.0 X institutional upper limit of normal;
   - Albumin ≥ 2.5 mg/dl;
   - Creatinine within normal institutional limits or creatinine clearance ≥ 60mL/min/1.73 m² for subject with creatinine levels above institutional normal;
   - Hemoglobin ≥ 9.0 g/dl (Note: The use of transfusion or other intervention to achieve Hgb ≥ 9.0 g/dl is acceptable.)
7. Patient must provide study specific informed consent prior to study entry;
8. Negative bHCG within 14 days prior to study entry if patient is pre or peri menopausa
NRG-GI001/LU207016

RANDOMIZED PHASE III STUDY OF FOCAL RADIATION THERAPY FOR UNRESECTABLE, LOCALIZED INTRAHEPATIC CHOLANGIOCARCINOMA

Exclusion Criteria:

1. Multiple lesions that don’t meet the criteria as satellite lesions
2. Extrahepatic metastases or malignant nodes beyond the periportal region.
   Celiac, pancreaticoduodenal and para-aortic nodes > 2 cm are ineligible. Note that benign
   nonenhancing periportal lymphadenopathy is not unusual in the presence of hepatitis and
   is permitted, even if the sum of enlarged nodes is > 2.0 cm;
3. Maximum diameter exceeding 12 cm (maximum diameter does not include satellite
   lesion);
4. Hepatic insufficiency resulting in clinical jaundice, encephalopathy and/or variceal bleed
   within 60 days prior to study entry;
5. Prior radiotherapy to the region of the liver that would result in overlap of radiation
   therapy fields;
6. Prior selective internal radiotherapy/hepatic arterial Yttrium therapy, at any time;
7. Direct tumor extension into the stomach, duodenum, small bowel or large bowel;
8. Measureable common or main branch biliary duct involvement with HCC;
9. Prior invasive malignancy (except non-melanomatous skin cancer) unless disease free for
   a minimum of 3 years. (Note: carcinoma in situ of the breast, oral cavity, or cervix is all
   permissible);
10. Prior systemic chemotherapy for the study cancer; note that prior chemotherapy for a
    different cancer is allowable;
11. Currently receiving other anti-cancer agents;
12. Participants who require anticoagulation should receive low-molecular weight or
    standard heparin and not warfarin;
13. Prior surgery for the IHC. (Liver resection is not allowed);
14. Severe Severe hepatic disease, defined as a diagnosis of Child-Pugh Class B or C hepatic
    disease;
15. Prior allergic reactions attributed to compounds of similar chemical or biologic
    composition to gemcitabine or cisplatin;
16. Severe, active co-morbidity, defined as follows:
   • Unstable angina and/or congestive heart failure requiring hospitalization within
     the last 6 months;
   • Transmural myocardial infarction within the last 6 months;
   • Acute bacterial or fungal infection requiring intravenous antibiotics at the time of
     registration;
   • Chronic Obstructive Pulmonary Disease exacerbation or other respiratory illness
     Requiring hospitalization or precluding study therapy within 30 days before
registration;

- HIV positive with CD4 count < 200 cells/microliter. Note that patients who are HIV positive are eligible, provided they are under treatment with highly active antiretroviral therapy (HAART) and have a CD4 count ≥ 200 cells/microliter within 30 days prior to registration. Note also that HIV testing is not required for eligibility for this protocol;

- End-stage renal disease (ie, on dialysis or dialysis has been recommended).

17. Pregnancy or women of childbearing potential and men who are sexually active and not willing/able to use medically acceptable forms of contraception; this exclusion is necessary because the treatment involved in this study may be significantly teratogenic;

18. Grade 3 or higher peripheral neuropathy