Study of NALIRIFOX in Advanced Unresectable Small Bowel Tumors

Status: RECRUITING

Eligibility Criteria

Age: 18 years and over

This study is NOT accepting healthy

Healthy Volunteers: volunteers

Inclusion Criteria:

1. Subject has been informed about the nature of the study, and has agreed to participate in the study, and signed the ICF prior to participation in any study-related activities. Also, as determined by the enrolling physician or protocol designee, ability of the subject to understand and comply with study procedures for the entire length of the study. 2. Age ≥ 18 years at the time of consent. 3. ECOG Performance Status of ≤ 1 within 28 days prior to registration and within 7 days prior to start of study regimen. 4. Histological or cytologically confirmed small bowel adenocarcinoma per AJCC, 9th edition that has not been previously treated in the metastatic setting. Subjects treated in the adjuvant setting who completed treated \> 6 months and do not have residual toxicities \> Grade 1 are eligible. NOTE: Subjects with only localized disease or disease which will likely become resectable after chemotherapy (per investigator discretion) are NOT eligible. 5. Mismatch repair proficient (MMRp) and/or microsatellite stable (MSS) disease per institutional standard of care testing. 6. Subject has one or more metastatic lesions measurable by CT scan (or MRI, if the subject a. is allergic to CT contrast media) according to RECIST Version 1.1 criteria. Lesions in a prior radiation field must have progressed subsequent to radiotherapy to be considered measurable. 7. Demonstrate adequate organ function as defined below. All screening labs to be obtained within 28 days prior to registration and repeated within 7 days prior of C1D1. * Platelets (Plt) ≥ 100,000 cells/mm3 * Absolute Neutrophil Count (ANC) ≥ 1,500 cells/mm3; without the use of hemopoietic growth factors * Hemoglobin (Hgb) ≥ 9 g/dL * Calculated creatinine clearance ≥ 30 mL/min; Cockcroft-Gault formula for actual body weight should be used for calculation. For subjects with a body mass index (BMI) \> 30 kg/m2, adjusted body weight should be used instead * Total bilirubin ≤ 1.5 × ULN * Aspartate aminotransferase (AST) ≤ 2 × ULN; \< 5× with liver metastases * Alanine aminotransferase (ALT) ≤ 2 × ULN; \< 5× with liver metastases * Albumin ≥ 2.5 gm/dL * PT and PTT ≤ 1.5 x ULN; subjects on warfarin or other vitamin K antagonists should be discussed with the sponsor-investigator. * Urinalysis: Urinalysis results without clinically significant abnormalities, per the investigator's assessment 8. Electrocardiogram (ECG) without any clinically significant findings (QT interval corrected by Fridericia's formula (QTcF) ≤450 msec and no known arrhythmias) and per the investigator's assessment. 9. Females of childbearing potential must have a negative urine or serum pregnancy test within ≤ 7 days prior to registration. If a urine test is done and it is positive or cannot be confirmed as negative, a serum pregnancy test will be required. 10. Females of childbearing potential who are sexually active with a male able to father a child must be willing to abstain from penile-vaginal intercourse or use an effective method(s) of contraception. Males able to father a child who are sexually active with a female of childbearing potential must be willing to abstain from penile-vaginal intercourse or use an effective method(s) of contraception. 11. Subjects infected with human immunodeficiency virus (HIV) are eligible if they meet all the following criteria: * CD4 count is ≥350 cells/uL, viral load is undetectable, and not taking prohibited cytochrome (CYP)-interacting medications; * Probable long-term survival with HIV if cancer were not present; * Stable on a highly active antiretroviral therapy (HAART) regimen for ≥ 4 weeks and willing to adhere to their HAART regimen with minimal overlapping toxicity and drug-drug interactions with the experimental agents in this study; * HIV is not multi-drug resistant; * Taking medication and/or receiving antiretroviral therapy that does not interact or have overlapping toxicities with the study medication. NOTE: Testing is not required at screening unless mandated by local policy. 12. Subjects with known chronic hepatitis B virus (HBV) infection, must have an undetectable HBV viral load on suppressive therapy, if indicated. Subjects with a history of hepatitis C virus (HCV) infection must have been treated and cured. For subjects with HCV infection who are currently on treatment, the HCV viral load must be undetectable to be eligible for this trial. NOTE: Testing is not required at screening unless mandated by local policy.

Exclusion Criteria:

1. Adenocarcinoma originating in the ampulla or appendix (duodenal tumors that involve the ampulla but originate in the duodenum are eligible). 2. Neuroendocrine or any other histology different than adenocarcinoma. 3. Prior treatment with irinotecan. 4. Prior treatment of SBA in the metastatic setting with surgery, radiotherapy, chemotherapy or investigational therapy: * Palliative radiotherapy is permitted but lesions in a prior radiation field must have progressed subsequent to radiotherapy to be considered measurable. * Placement of biliary stent/tube is permitted. 5. Known history of central nervous system (CNS) metastases. (subjects on a stable or decreasing dose of steroids and deemed clinically stable as per the investigator's assessment are eligible). 6. Clinically significant gastrointestinal disorder including hepatic disorders, bleeding, inflammation, occlusion, diarrhea \> Grade 1, malabsorption syndrome, ulcerative colitis, inflammatory bowel disease, or partial bowel obstruction. 7. Pregnant or breastfeeding. NOTE: breast milk cannot be stored for future use while the mother is being treated on study. 8. History of any second malignancy in the last 2 years; subjects with prior history of in-situ cancer or basal or squamous cell skin cancer are eligible. Subjects with a history of other malignancies are eligible if they have been continuously disease free for at least 2 years prior to screening. Subjects who have a concurrent malignancy that is clinically stable and does not require tumor-directed treatment are eligible. 9. Known hypersensitivity to any of the components of nanoliposomal irinotecan, other liposomal products, or any components of 5-FU, LV or oxaliplatin. 10. Concurrent illnesses that would be a relative contraindication to trial participation such as active cardiac or liver disease, including: * Severe arterial thromboembolic events (myocardial infarction, unstable angina pectoris, stroke) less than 6 months before screening * High cardiovascular risk, including, but not limited to, recent coronary stenting or myocardial infarction in the past year prior to screening * New York Heart Association (NYHA) Class III or IV congestive heart failure, ventricular arrhythmias or uncontrolled blood pressure 11. Active infection or an unexplained fever \>38.5°C during screening visits or on the first scheduled day of dosing (at the discretion of the investigator, subjects with tumor fever may be enrolled), which in the investigator's opinion might compromise the subject's participation in the study or affect the study outcome. 12. Major surgery, other than diagnostic surgery, within 4 weeks prior to consent. 13. Use of strong inhibitors or inducers of CYP3A, CYP2C8 and UGT1A1. Subjects are ineligible if: * they are unable to discontinue the use of strong inhibitors of CYP3A, CYP2C8 and UGT1A1 at least 1 week prior to consent; * they are unable to discontinue the use of strong CYP3A and CYP2C8 inducers at least 2 weeks prior to consent; 14. There is presence of any contraindications outlined in the Contraindications or Warnings and Precautions sections of the IB for nanoliposomal irinotecan, or in the prescribing information for 5-FU, LV or oxaliplatin. 15. Subjects who, in the opinion of the investigator, have symptoms or signs suggestive of clinically unacceptable deterioration of the primary disease at the time of screening. 16. History of systemic connective tissue disorders (e.g. lupus, scleroderma, arteritis nodosa). 17. Subjects who have received a live vaccine within 4 weeks prior to consent. 18. History of the following: interstitial lung disease, slowly progressive dyspnea and unproductive cough, sarcoidosis, silicosis, idiopathic pulmonary fibrosis, pulmonary hypersensitivity pneumonitis or multiple allergies, and peripheral artery disease (e.g. claudication, Leo Buerger's disease). 19. Known low or absent dihydropyridine dehydrogenase (DPD) activity. This is not mandatory but where required by local regulations, testing for DPD deficiency must be performed using a validated method which is recommended by local health authorities.

Conditions & Interventions

Interventions:

DRUG: Nanoliposomal irinotecan, DRUG: Oxaliplatin, DRUG: 5 fluorouracil, DRUG: Leucovorin

Conditions:

Small Bowel Adenocarcinoma

More Information

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