Protocol Title: A Phase II Clinical Trial Platform of Sensitization Utilizing Total Neoadjuvant Therapy (TNT) in Rectal Cancer.

Target Population: Rectal Adenocarcinoma / Stage II – Stage III Rectal Cancer

Summary: This randomized phase II trial studies how well veliparib works with combination chemortherapy and radiation therapy in treating patients with rectal cancer that has spread from where it started to nearby tissue or lymph nodes (locally advanced).

Key Inclusion Criteria:
- Diagnosis of adenocarcinoma of the rectum with the major portion of the tumor intact.
  - Prior to randomization, the investigator must specify and document the following:
    - Distance of lowest tumor margin from the anal verge.
    - Intent of sphincter sparing surgical resection or not according to the primary surgeon.
- The tumor must be clinically determined to be locally advanced stage II or III rectal cancer, defined as meeting any ONE of the following criteria:
  - Distal location: cT3-4 =< 5 cm from the anal verge, any N.
  - Bulky: any cT4 with the majority of the untreated tumor < 12 cm from the anal verge or below the peritoneal reflection as determined by the treating surgeon, or evidence that the tumor is adjacent to (defined as within 3 mm of) the mesorectal fascia on MRI or ERUS/pelvic CT (with IV contrast) scan.
  - High risk for metastatic disease with 4 or more regional lymph nodes (cN2).
  - Not a candidate for sphincter-sparing surgical resection prior to neoadjuvant therapy.
- At least two untreated core biopsy specimens from the untreated tumor (formalin-fixed, paraffin-embedded [FFPE]) must have been collected previously and be available for submission per protocol requirements.
- ECOG Performance Score of 0-2.
- Patients with AIDS-related illnesses or HIV must:
  - Have a CD4 count ≥ 200 cells/uL within 30 days before beginning study therapy.
  - Be off all antiretroviral therapy > 60 days before beginning study and no evidence of infection.
- Pregnancy test done within 14 days before randomization must be negative.

Key Exclusion Criteria:
- Rectal cancer histology other than adenocarcinoma.
- Definitive clinical or radiologic evidence of metastatic disease.
- History of prior invasive rectal malignancy, regardless of disease-free interval.
- Cardiac disease that would preclude that use of any of the drugs included in the GI002 treatment regimen.
- Sensory or motor neuropathy ≥ grade 2.
- Inflammatory bowel disease or history of abdominal surgery that may interfere with GI motility or absorption.
- Active seizure disorder uncontrolled by medication.
- Any antineoplastic therapy for this cancer before randomization.
- Synchronous colon cancer.
- Other invasive malignancy within 5 years before randomization; exceptions are colonic polyps, non-melanoma skin cancer or carcinoma-in-situ of the cervix.
- Chemotherapy within 5 years before randomization OR major surgery within 4 weeks before randomization.
- Any therapeutic pelvic radiation.

Contacts:
Principal Investigator: Suma Satti, MD
Research Nurses (RN): Amanda Woolery (amanda.woolery@ochsner.org, ext. 20275)
Sharon Jerdonek (sharon.jerdonek@ochsner.org, ext. 23929)

For additional information: https://clinicaltrials.gov/ct2/show/NCT02921256