Protocol Title: Colorectal Cancer Metastatic dMMR Immuno-Therapy (COMMIT) Study: A Randomized Phase III Study of mFOLFOX6/Bevacizumab Combination Chemotherapy with or without Atezolizumab or Atezolizumab Monotherapy in the First-Line Treatment of Patients with Deficient DNA Mismatch Repair (dMMR) Metastatic Colorectal Cancer

Target Population: Deficient DNA Mismatch Repair (dMMR) Metastatic Colorectal Cancer

Summary: This randomized phase III trial studies how well combination chemotherapy, Bevacizumab, and/or Atezolizumab work in treating patients with dMMR Metastatic Colorectal Cancer.

Key Inclusion Criteria:
• Diagnosis of Metastatic Adenocarcinoma of Colon or Rectum without previous chemotherapy or any other systemic therapy for Metastatic Colorectal Cancer.
• Tumor determined to be dMMR by CLIA-certified IHC assay with a panel of all four IHC markers, including MLH1, MSH2, PMS2, and MSH6.
• Adequate amount of archived tumor tissue, either from primary Colorectal Cancer site or metastatic lesions, for central confirmation of dMMR status either whole or part of FFPE block or ≥ 8 unstained slides.
• Documentation by PET/CT scan, CT scan, or MRI that the patient has untreated measurable metastatic disease.
• No immediate need for surgical intervention for the primary tumor or palliative diversion/bypass.
• For women of childbearing age, pregnancy test done within 14 Days prior randomization must be negative.

Key Exclusion Criteria:
• Patients with CNS metastases are excluded (with specific exceptions).
• Uncontrolled high blood pressure defined as SBP > 150 mmHg or DBP > 90 mmHg ± anti-hypertensives.
• Serious or non-healing wound, skin ulcer, or bone fracture.
• History of TIA, CVA, GI perforation, or arterial thrombotic event within 6 Months prior to randomization or symptomatic peripheral ischemia.
• Other malignancies are excluded unless the patient has completed therapy for the malignancy ≥ 12 Months prior to randomization and is considered disease-free.
• Known dihydro pyrimidine dehydrogenase (DPD) deficiency.
• Symptomatic peripheral sensory neuropathy ≥ grade 2 in patients with no prior Oxaliplatin therapy.
• Prior treatment with Oxaliplatin chemotherapy within 6 Months prior to randomization.
• Prior treatment with anti-PD-1, or anti-PD-L1 therapeutic antibody or pathway-targeting agents.
  o Patients with prior treatment of anti-CTLA-4 may be enrolled provided specific requirements are met.
• Treatment with systemic immunostimulatory medications within 42 Days prior to randomization.
• Patients taking bisphosphonate therapy for symptomatic hypercalcemia; use of bisphosphonate therapy for other reasons (e.g., bone metastasis or osteoporosis) is allowed.
• Patient requiring treatment with RANKL inhibitor who cannot discontinue before treatment with Atezolizumab.
• History of idiopathic pulmonary fibrosis, pneumonitis, organizing pneumonia, evidence of active pneumonitis on screening chest CT scan, or known active tuberculosis.
• Administration of a live, attenuated vaccine within 28 Days prior to randomization or anticipation that a live, attenuated vaccine will be required during the study and up to 5 Months after the last dose of Atezolizumab.
• Psychiatric illness/social situations that would limit compliance with study requirements.
• Patients with prior allogeneic bone marrow transplantation or prior solid organ transplantation.

Contacts:
Principal Investigator: Suma Satti, MD
Research Nurses (RN): April Wendt (awendt@ochsner.org, ext. 24548)
  Sharon Jerdonek (sharon.jerdonek@ochsner.org, ext. 23929)

For additional information: https://clinicaltrials.gov/ct2/show/NCT02997228

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