Title: NCCTG N0949: Randomized Phase III Trial of mFOLFOX7 or XELOX Plus Bevacizumab Versus 5-Fluorouracil/Leucovorin or Capecitabine Plus Bevacizumab as First-line Treatment in Elderly Patients with Metastatic Colorectal Cancer.

Purpose: To compare the length of time during and after treatment that metastatic colorectal cancer does not get worse in older patients treated with bevacizumab plus either 5-fluorouracil/leucovorin or capecitabine without oxaliplatin or in patients treated with bevacizumab plus 5-fluorouracil/leucovorin or capecitabine with oxaliplatin.

Eligibility: Randomization – Inclusion Criteria
- Age ≥ 70 years (age 70-74 years limited to no greater than 25% of the whole study population and eligibility will be modified at the time this benchmark is reached).
- Patients must have metastatic colorectal cancer that has been histologically or cytologically confirmed. Confirmation may be from either the primary tumor or a metastasis.
- Eastern Cooperative Oncology Group Performance Status (ECOG PS) 0, 1, or 2. ECOG PS criteria are on the NCCTG website at https://ncctg.mayo.edu/ncctg/forms/NonProtocolSpecificForms.
- The following laboratory values obtained <14 days prior to randomization.
  • Absolute neutrophil count (ANC) ≥ 1,500/mm3
  • Peripheral Platelet Count (PLT) ≥ 100,000/mm3
  • Hemoglobin (HgB) > 9.0 g/dL
  • Total bilirubin ≤1.5 x upper limit of normal (ULN)
  • Aspartate transaminase (AST) ≤2.5 x ULN (<5 x ULN for patients with liver involvement)
  • Alkaline phosphatase ≤3 x ULN (<5 x ULN for patients with liver involvement)
  • Creatinine <1.5 x ULN
  • INR <1.5 x ULN unless patients are receiving anti-coagulation therapy. Patients receiving prophylactic anti-coagulation therapy with an agent such as warfarin or heparin are allowed to participate if INR ≤3.0.
  • UPC ratio ≤1 or urine dipstick ≤2+. NOTE: Urine protein must be screened by urine analysis for Urine Protein Creatinine (UPC) ratio or by dipstick. For UPC ratio ≥1.0 or urine dipstick ≥2+, 24-hour urine protein must be obtained and the level should be <1000 mg.
- Life expectancy ≥3 months.
- Ability to complete questionnaire(s) by themselves or with assistance.
- Provide informed written consent.
- Willing to provide mandatory blood samples for correlative research purposes N0949 29 Addendum 1 (see Sections 6.0 and 14.0).

Randomization – Exclusion Criteria
- The following because this study involves agents whose genotoxic, mutagenic and teratogenic effects on the developing fetus and newborn are unknown:
  • Men of childbearing potential who are unwilling to employ adequate
contraception
- Co-morbid systemic illnesses or other severe concurrent disease which, in the judgment of the investigator, would make the patient inappropriate for entry into this study or interfere significantly with the proper assessment of the safety and adverse events of the prescribed regimens.
- Immunocompromised patients (other than that related to the use of corticosteroids) including patients known to be HIV positive with CD4<100 cells/μL.
- Uncontrolled intercurrent illness including, but not limited to, ongoing or active infection, symptomatic congestive heart failure, unstable angina pectoris, cardiac arrhythmia, or psychiatric illness/social situations that would limit compliance with study requirements.
- Receiving any other investigational agent which would be considered as a treatment for the primary neoplasm.
- Other active malignancy ≤ 3 years prior to randomization. EXCEPTIONS: Nonmelanotic skin cancer or carcinoma-in-situ of the cervix. NOTE: If there is a history of prior malignancy, patients must not be receiving other specific treatment (other than hormonal therapy) for this prior cancer.
- Prior chemotherapy, radiation therapy, immunotherapy, or biological therapy for recurrent or metastatic colorectal cancer. (NOTE: Prior chemotherapy or radiotherapy is permitted if they had been administered as adjuvant or neoadjuvant therapy and a complete surgical resection of the original colorectal cancer had been achieved.)
- Progressive disease ≤12 months of completing oxaliplatin-containing adjuvant therapy.
- Prior radiation to >30% of the bone marrow at any time.
- Calculated creatinine clearance <60 mL/minute.

TO CALCULATE CREATININE CLEARANCE (CrCl) from SERUM CREATININE:

\[ \text{CrCl} = \frac{(140 - \text{age}) \times \text{wt. in kg} \times 0.85 \text{ (female)} \text{ OR} \times 1.00 \text{ (male)}}{72 \times \text{serum creatinine}} \]

Note: If calculated creatinine clearance does not meet eligibility requirement, a 24 hour urine can be collected for a creatinine clearance, and the patient can be enrolled if measured creatinine clearance ≥ 60 mL/minute.

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Approved Enrollment Number: 20
Current Enrollment: 0