Version 09/03/21 (Add. #1)

NCI National Clinical Trials Network

EA2201

ECOG-ACRIN cancer research group
Reshaping the future of patient care

For Patients with Rectal Adenocarcinoma

EA2201 Available Through ECOG-ACRIN Cancer Research Group

A Phase II Study of Neoadjuvant Nivolumab plus Ipilimumab and Short-Course Radiation In MSI-H/dMMR Locally Advanced Rectal Adenocarcinoma

Patient Population

See Section 3.0 for Complete Eligibility Details

- Age ≥ 18 years, ECOG PS 0-2, adequate lab values
- Must have histologically confirmed adenocarcinoma of the rectum with the inferior margin within 15 cm from the anal verge based on colonoscopy and/or flexible sigmoidoscopy
- Must have T3-4Nx or TxN+ disease (Stage II/III) based on MRI of the pelvis and computed tomography of the chest and abdomen, done within 28 days of registration
- Must have MSI-H or dMMR tumors based on immunohistochemistry/PCR
- No previous chemo/immunotherapy for rectal cancer; no previous radiotherapy to the pelvis
- No major surgery within 28 days of registration
- No history of interstitial lung disease/evidence of interstitial lung disease on baseline chest CT
- No serious active infection requiring IV antibiotics at time of registration
- No active autoimmune disease/history of autoimmune disease that might recur, which may affect vital organ function or require immune suppressive treatment (see protocol)
- No condition requiring systemic treatment with either corticosteroids/other immunosuppressive medications within 14 days prior to registration (see protocol)
- Patients should have urine dipstick with proteinuria < 1 (see protocol for details)
- HIV, HBV, HCV patients permitted per protocol
- Patients with known history/current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should be NYHA class 2B or better
- Must not have had live vaccines within 30 days of registration (see protocol for details); must agree to not receive live vaccines while on this study

Treatment Plan

See Section 5.0 for Complete Treatment Details

Induction Phase (Neoadjuvant Immunotherapy and Radiation):

- Immunotherapy (2 cycles; 28 days each) prior to RT
  - ◊ Nivolumab 480 mg (30 min IV) followed by ipilimumab 1 mg/kg (90 minute IV)
- 5 Gy x 5 fractions; RT to start 2-6 weeks after completion of cycle 2 of nivolumab/ipilimumab
- Immunotherapy (2 cycles) after RT; cycle 3 to start 2-6 weeks after completion of RT
  - ◊ Nivolumab 480 mg (30 min IV) followed by ipilimumab 1 mg/kg (90 minute IV)
- Reassessment prior to surgical resection (digital rectal exam [DRE], MRI pelvis, CT chest/abdomen, sigmoidoscopy with optional biopsy)

Surgical Treatment:

- Total mesorectal excision (TME) with standardized technique
- Surgery to occur 8-12 weeks after completion of 4th cycle of nivolumab/ipilimumab

Adjuvant Therapy:

- To be given at the discretion of the physician

Notes:

- *After the completion of therapy, patients will be followed for at least 5 years*
- *See protocol section 5.2 for RT details*
  - ◊ *IMRT is permitted but not required; credentialing is required for IMRT*
  - ◊ *6 MV is required*
  - ◊ *Tomotherapy delivery is allowed*
  - ◊ *Proper immobilization is important; CT simulation is required*

Study Chair:
Kristen Ciombor, MD

Co-Chair:
Cathy Eng, MD

Patient Enrollment

All Sites: Oncology Patient Enrollment Network (OPEN), https://open.ctsu.org

Protocol Information

ECOG-ACRIN Operations-Boston: 857-504-2900, http://ecog-acrin.org (Member Login)

Please Enroll Your Eligible Patients!

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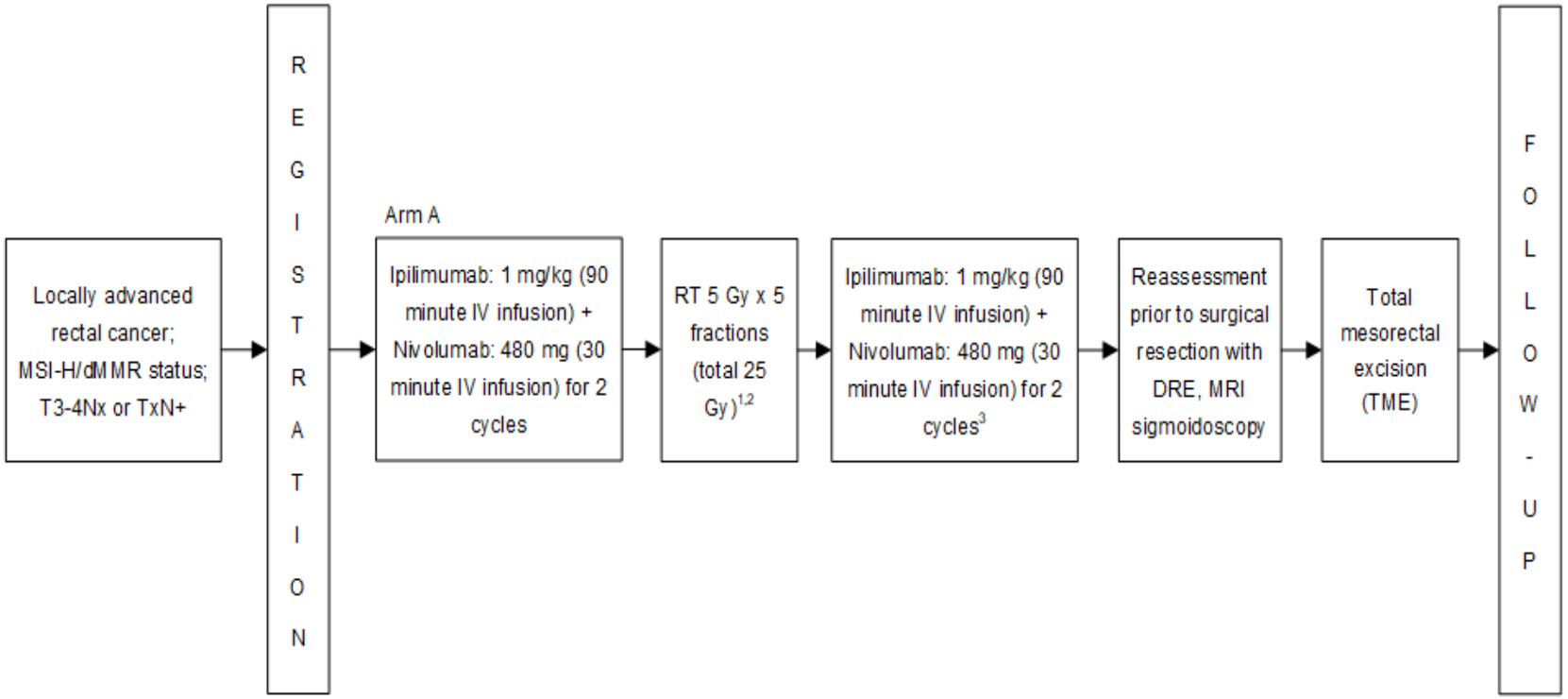
Schema



1 cycle = 28 days

Accrual Goal: 31

1. Please see Section 5.2 for details of radiation therapy.
2. Radiation to start at least 2 weeks but no longer than 6 weeks after completion of cycle 2 of nivolumab/ipilimumab.
3. Cycle 3 of nivolumab/ipilimumab to start within 2-6 weeks of completion of radiation therapy.