

Fast Facts

S0820: A Double Blind Placebo-Controlled Trial of Eflornithine and Sulindac to Prevent Recurrence of High Risk Adenomas and Second Primary Colorectal Cancers in Patients with Stage 0-III Colon or Rectal Cancer, Phase III

Eflornithine and Sulindac and placebo provided
AJCC Staging 6th ed; CTCAE v.4

Step 0: Registration (Optional)

1. Patients with a primary colon or rectal cancer resection who are potentially eligible for S0820 may be pre-registered at Step 0.
 - Patients registered to Step 0 will appear on an institutional patient tracking report (see Section 13.0). Patients registered to Step 0 are not registered to the S0820 protocol. To participate in S0820, patients must be registered to Step 1 after patient is consented and evaluation of eligibility per protocol Section 5.2. Patients registered to S0820 at Step 0 continuing to Step 1 registration must use the same SWOG patient ID for registration to S0820 Step 1.

Step 1: Registration

1. Patients must have a history of Stage 0, I, II or III colon or rectal adenocarcinoma that has been treated per standard care with resection alone or in combination with radiation or chemotherapy. (32) Adjuvant chemotherapy and RT treatment must have been completed at least 30 days prior to registration.
2. Only patients with history of segmental resections are eligible (i.e. right colectomy, extended right colectomy, transverse colectomy, left colectomy, extended left colectomy, sigmoid colectomy, low anterior resection, abdominoperineal resection). The definition of resection does not include endomucosal resection (EMR). Patients that have received total proctocolectomy are ineligible.

For Tis (Stage 0) or pT1 patients only, resection may consist entirely of polypectomy (without completion of partial colectomy) if ALL of the following criteria are met:

- Single specimen, completely removed.
 - Clear margins
 - None of the following must be present:
 - Moderate or poor differentiation
 - Lymphovascular invasion
 - Perineural invasion
3. Patients must be registered between 180 days and 456 days (inclusive) of primary resection. Patients must show no evidence of disease (NED) based on post-operative colonoscopy (performed at least 180 days after the colon resection date or at least 120 days after the rectal resection date and prior to registration) and CT scans* of chest, abdomen and pelvis (performed at least 180 days after the colon resection date or at least 120 days after the rectal resection date and prior to registration). Patients with adenomas detected at the one-year postoperative colonoscopy are eligible if all adenomas have been completely removed. (*CT scan is for high risk patients, as per NCCN guidelines and at the discretion of the treating physician.) **NOTE:** MRI evaluation is an acceptable alternative to CT scans for eligibility purposes.
 4. Patients must be at least 18 years of age
 5. Patients must not have cardiovascular risk factors including unstable angina, history of documented myocardial infarction or cerebrovascular accident, coronary artery bypass surgery, or New York Heart Association Class III or IV heart failure. Patients must not have known uncontrolled hyperlipidemia (defined as LDL-C \geq 190 mg/dL or triglycerides \geq 500 mg/dL) within the last 3 years

prior to registration or uncontrolled high blood pressure (systolic blood pressure > 150 mm Hg) within 28 days prior to registration. (A table of New York Heart Association Classifications is included in Appendix 19.6.)

6. Patients must not have a known history of familial adenomatous polyposis, hereditary nonpolyposis colorectal cancer, or inflammatory bowel disease.
7. Patients must have a pure tone audiometry evaluation to document air conduction within 30 days prior to registration. Patients with hearing loss >40 dB in any of the five tested frequencies (250 Hz, 500 Hz, 1,000 Hz, 2,000 Hz, 4,000 Hz) are not eligible. Patients with active ear infections should be tested only after the acute phase of infection has resolved. For optimal results, it is recommended that testing be conducted by an audiologist, in a hearing test room, with insert earphones. Submit S0820 Audiometry Evaluation Form per Section 14.5.
Note: Sites should not order audiometry evaluation until the potential participant has met all other eligibility criteria required for this study.
8. Patients must not have known hypersensitivity to eflornithine or sulindac or the excipients byproducts. Patients must not have experienced asthma, urticaria, or allergic-type reactions after taking aspirin or other NSAID.
9. Patients must not have documented history of gastric/duodenal ulcer within the last 12 months. Participant must not currently be on treatment for gastric/duodenal ulcer or be experiencing symptoms at study entry. Patients with gastroesophageal reflux disease (GERD) are eligible, however, and these patients may receive over-the-counter histamine-2 (H2) antagonists, protonpump inhibitors, or other prescription-based treatment for GERD.
10. Patients must have a Zubrod Performance Status of 0 – 1 (see Section 10.3).
11. Patients must not be expecting to receive radiation or additional chemotherapy.
12. Patients must not be receiving or plan to receive concomitant corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), nor anticoagulants on a regular or predictable intermittent basis. (NSAID use may not exceed 10 days per month.) Patients may receive daily aspirin for cardiovascular prophylaxis as long as ASA is ≤ 100 mg per day or \leq two 325 mg tablets per week.
13. Patients must have the ability to swallow oral medication.
14. Patients must have no significant medical or psychiatric condition that would preclude study completion. Tests and exams for this determination should be completed within 28 days prior to registration.
15. Patients must have adequate blood counts as evidenced by the following results, obtained within 28 days prior to registration:
total WBC $\geq 4.0 \times 10^3/\text{mcL}$, platelets $\geq 100,000/\text{mcL}$ and hemoglobin > 11.0 g/dL.
16. Patients must have adequate liver function as evidenced by the following results, obtained within 28 days prior to registration: serum bilirubin ≤ 2.0 mg/dL and AST (SGOT) or ALT (SGPT) $\leq 2 \times$ IULN (institutional upper limit of normal).
17. Patients must have adequate kidney function as evidenced by serum creatinine $\leq 1.5 \times$ IULN obtained within 28 days prior to registration.
18. No other prior malignancy (i.e., other than as noted in Section 5.2a.1) is allowed except for adequately treated basal cell or squamous cell skin cancer, in situ cervical cancer, or other cancer for which the patient has been disease-free for > 5 years.
19. Patients must not be pregnant or nursing (due to the status of eflornithine and sulindac as pregnancy class C agents). Women/men of reproductive potential must have agreed to use an effective contraceptive method. A woman is considered to be of "reproductive potential" if she has had menses at any time in the preceding 12 consecutive months. In addition to routine contraceptive methods, "effective contraception" also includes heterosexual celibacy and surgery intended to prevent pregnancy (or with a side-effect of pregnancy prevention) defined as a hysterectomy, bilateral oophorectomy or bilateral tubal ligation. However, if at any point a previously celibate patient chooses to become heterosexually active during the time period for use of contraceptive measures outlined in the protocol, he/she is responsible for beginning contraceptive measures.

Specimen Submission and Substudy Criteria

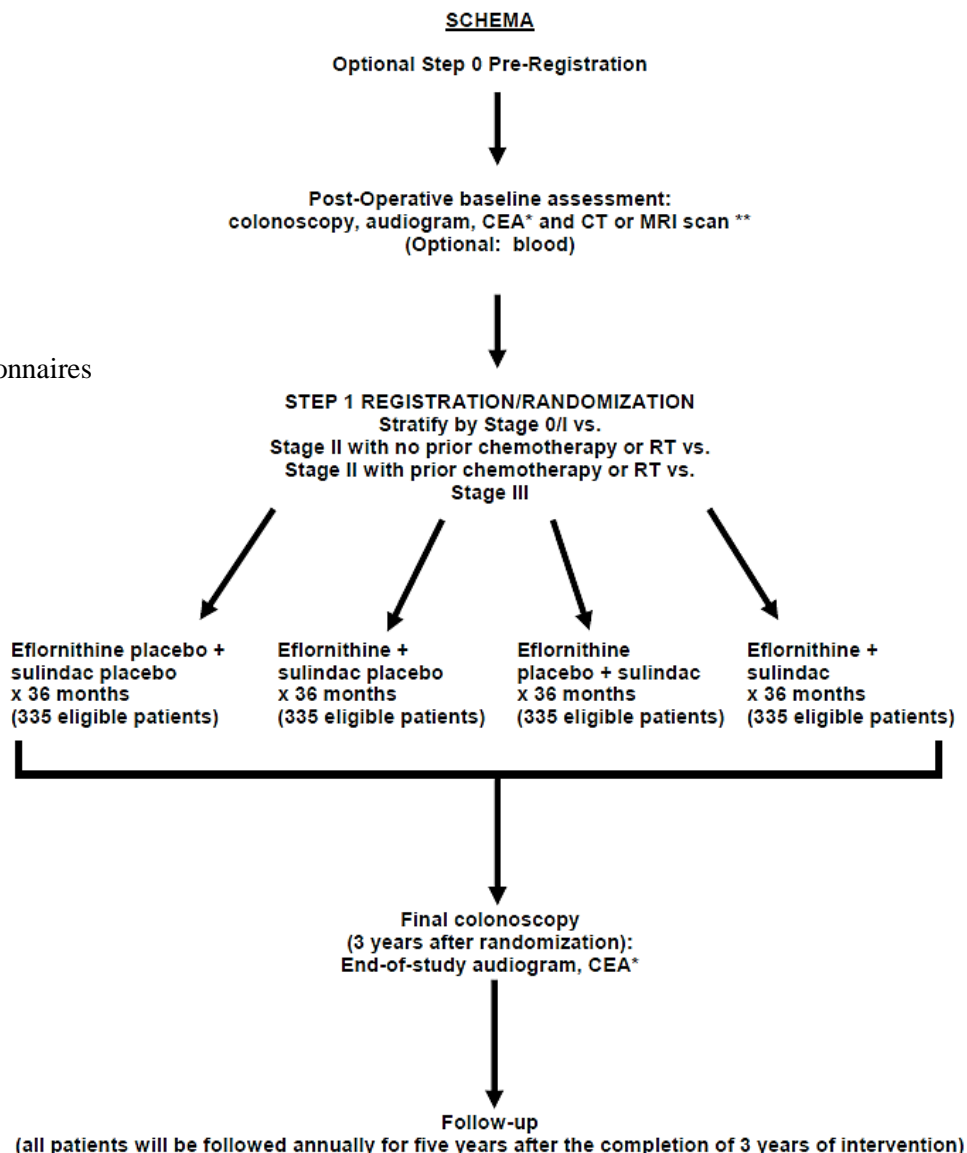
1. Patients must be offered the option to participate in submission of specimens for banking for future translational medicine studies (as specified in Section 15.1).
2. Patients participating through PK sites (listed on page 1a of the protocol), must be offered the option to submit blood specimens for population pharmacokinetic analysis (as specified in Appendix 19.5).
3. Patients must be offered the option to participate in the Diet and Lifestyle Substudy (as described in Section 15.2).

Regulatory Criteria

1. Individuals must not currently be participating in any other clinical trial for the treatment or prevention of cancer unless they are no longer receiving the intervention and are in the follow-up phase only. Patients must also agree not to join such a trial while participating in this study.
2. All patients must be informed of the investigational nature of this study and must sign and give written informed consent in accordance with institutional and federal guidelines.
3. As a part of the OPEN registration process (see Section 13.4 for OPEN access instructions) the treating institution's identity is provided in order to ensure that the current (within 365 days) date of institutional review board approval for this study has been entered in the system.

Pre-Study Parameters

- History & Physical
- Audiometry Evaluation
- CBC, WBC, Platelets
- CMP
- AST/ALT
- CEA
- Colonoscopy
- CT – chest/abd/pelvis
- Diet and Lifestyle questionnaires



* For patients with T3 or greater lesions or lymph node positive tumors

** In high-risk patients, per National Comprehensive Cancer Network (NCCN) guidelines and at the discretion of the treating physician.