

NSABP P-5: Statin Polyp Prevention Trial in Patients with Resected Colon Cancer

Fast Facts

Patient selection guidelines

Although the guidelines below are not inclusion/exclusion criteria, investigators should consider each of these factors when selecting patients for P-5. Investigators should also consider all other relevant factors (medical and non-medical), as well as the risks and benefits of the study therapy, when deciding if a patient is an appropriate candidate for P-5.

- Patients should have a life expectancy of at least 7 years, excluding their diagnosis of colon cancer. (Co-morbid conditions should be taken into consideration but not the diagnosis of colon cancer.)
- Patients must be willing to have follow-up colonoscopies at approximately 12, 36, and 60 months following randomization.
- Female patients and male patients with female partners of reproductive potential must agree to use an effective method of contraception during therapy and for at least 3 months after the last dose of study drug.
- Patients cannot have any psychiatric or addictive disorders or other conditions that, in the opinion of the investigator, would preclude the patient from meeting the study requirements.

Patient eligibility criteria

1. The patient must have consented to participate and must have signed and dated an appropriate IRB-approved consent form that conforms to federal and institutional guidelines.
2. Patients must be ≥ 18 years old.
3. Patients must have an ECOG performance status of 0 or 1 (see Appendix A).
4. Patients must have the ability to swallow oral medication.
5. Patients must have resected adenocarcinoma of the colon staged as AJCC Stage I or II.
6. Patients must have had surgical resection of the colon adenocarcinoma with curative intent within 1 year prior to randomization. (Laparoscopically-assisted colectomy is permitted.)
7. Patients must have completed any adjuvant therapy prior to randomization.
8. Patients who are taking cardioprotective low-dose aspirin at study entry must not have clinically significant toxicity, as determined by the investigator, that precludes continuation of aspirin, and the patient must be willing to continue aspirin therapy (81 mg or 325 mg) throughout study therapy.
9. Colonoscopy requirements *within 180 days prior to randomization*:
 - a. The patient must have either undergone a preoperative or postoperative documented colonoscopy to the cecum (or small bowel anastomosis) with adequate bowel preparation.
 - b. All observed polyps must have been removed. (Polyps can be removed during colonoscopy or surgery performed prior to randomization.)
10. Postoperative serum creatinine performed within 90 days prior to randomization must be $\leq 1.5 \times$ ULN for the lab.
11. The following criteria for evidence of adequate hepatic function based on postoperative testing performed within 90 days prior to randomization must be met:
 - a. AST *or* ALT $\leq 3.0 \times$ ULN for the lab, *and*
 - b. Total bilirubin $\leq 1.5 \times$ ULN for the lab

Note: If both AST and ALT were performed, both values must meet the 4.2.11 criterion.

Patient ineligibility criteria

1. Tumor with the distal border located < 12 cm from the anal verge.
2. Total colectomy or total proctocolectomy.
3. Classic Familial Adenomatous Polyposis, Attenuated Familial Adenomatous Polyposis (i.e., 20 or more adenomas, either synchronous or metachronous), or Hereditary Nonpolyposis Colorectal Cancer (Lynch Syndrome).
4. Malabsorption syndrome, ulcerative colitis, inflammatory bowel disease, resection of the stomach or small bowel, or other disease significantly affecting gastrointestinal function.
5. History of documented upper GI bleeding or upper GI ulcerative disease.
6. Statin use within 30 days prior to randomization.
7. Hyperlipidemia with clinical indication for statin therapy or other prescribed medication. Determination of acceptable fasting lipid values should be in accordance with current dyslipidemia management guidelines.

8. Unwillingness to discontinue chronic use of NSAIDs (other than cardioprotective low-dose aspirin 81 mg or 325 mg) prior to randomization.
9. Anticipated need for chronic use of NSAIDs (other than cardioprotective low-dose aspirin 81 mg or 325 mg).
10. Inadequately treated hypothyroidism, as determined by the investigator.
11. History of myopathy or rhabdomyolysis.
12. Hypersensitivity or intolerance to statins.
13. Chronic drug therapy with cyclosporine, coumarin anticoagulants, gemfibrozil, some other lipid-lowering therapies (fibrates or niacin), lopinavir/ritonavir, or drugs (such as ketoconazole, spironolactone, or cimetidine) that lower levels or activity of steroid hormones.
14. Pregnancy or lactation at the time of study entry. (Pregnancy testing must be performed within 14 days prior to randomization according to institutional standards for women of childbearing potential.)
15. Previous malignancies unless the patient has been disease-free for 5 or more years prior to randomization and is deemed by the physician to be at low risk for recurrence. Patients with the following cancers are eligible if diagnosed and treated within the past 5 years: all in situ cancers and basal cell and squamous cell carcinoma of the skin.
16. Other non-malignant systemic disease that would preclude a patient from receiving rosuvastatin or would prevent prolonged follow-up.
17. Administration of any investigational agent within 30 days before randomization.

Pre-study Parameters

1. History and physical exam including GI history, height, weight, performance status, colon cancer family history assessment; Calcium and Vitamin D use assessment
2. Serum Creatinine, total bilirubin, AST or ALT, fasting lipid panel (triglycerides, total cholesterol, LDL-C, HDL-C), pregnancy test if applicable
3. Colonoscopy within 180 days.

Treatment

