

FAST FACTS

ALLIANCE A021703

RANDOMIZED DOUBLE-BLIND PHASE III TRIAL OF VITAMIN D3 SUPPLEMENTATION IN PATIENTS WITH PREVIOUSLY UNTREATED METASTATIC COLORECTAL CANCER (SOLARIS)

Eligibility Criteria

1. Documentation of Disease:

Histologically confirmed advanced/metastatic colorectal adenocarcinoma for which metastasectomy is not planned.

No known dMMR or MSI-H disease.

2. Measurable disease per RECIST v1.1 as defined in [Section 11.0](#).

3. Prior Treatment

a. No prior systemic treatment for metastatic disease.

b. Patients may have received prior neoadjuvant or adjuvant chemotherapy and/or chemoradiation. The last course of adjuvant therapy must have been completed > 12 months prior to colorectal cancer recurrence.

c. Patients may have received prior standard rectal cancer chemoradiation. Previous radiation therapy must have been completed ≥ 4 weeks prior to registration.

d. No continuous daily use of vitamin D supplements $\geq 2,000$ IU per day for the 12 months prior to registration. Patients may have had continuous daily use of vitamin D supplements $\geq 2,000$ IU per day if total duration < 12 months in the 12 months prior to registration. Patients may have had continuous daily use of vitamin D supplements < 2,000 IU per day for any duration prior to registration.

e. Patients must have completed any major surgery or open biopsy ≥ 4 weeks prior to registration and must have completed any minor surgery or core biopsy ≥ 1 week prior to registration. (Note: insertion of a vascular access device is not considered major or minor surgery.) Patients must have recovered from the effects of any surgery (e.g. wound is healed, no active infection, no drains, etc.) prior to registration.

4. Not pregnant and not nursing.

a. This study involves an agent that has known genotoxic, mutagenic and teratogenic effects. Therefore, for women of childbearing potential only, a negative serum or urine pregnancy test done ≤ 14 days prior to registration is required.

5. Age ≥ 18 years

6. ECOG Performance Status: 0-1

7. Required Initial Laboratory Values:

- Absolute Neutrophil Count $\geq 1,500/\text{mm}^3$
- Platelet Count $\geq 100,000/\text{mm}^3$
- Hemoglobin ≥ 9 g/dL

- Creatinine ≤ 1.5 x upper limit of normal (ULN)
OR
Calc. CrCl > 30 mL/min
 - Calcium ≤ 1.0 x ULN *
 - Total Bilirubin ≤ 1.5 x ULN**
 - AST/ALT ≤ 2.5 x ULN ***
 - UPC Ratio < 1 mg/dL
OR
Urine Protein $\leq 1+$ ****
- *Corrected for albumin level if albumin not within institutional limits of normal
 ** If Gilbert's disease, use direct bilirubin instead of total bilirubin; direct bilirubin ≤ 1.5 x ULN if patient to receive FOLFIRI; direct bilirubin ≤ 3.0 x ULN if patient to receive mFOLFOX6
 *** AST/ALT < 5 x ULN if clearly attributable to liver metastases
 ****If urine protein is above 1, then 24-hour urine must be greater than or equal to 1 g/24hours.

8. Patient History

- a. No resectable metastatic disease for which potentially curative metastasectomy is planned.
- b. No "currently active" second malignancy other than non-melanoma skin cancers or cervical carcinoma in situ. Patients are not considered to have a "currently active" malignancy if they have completed therapy and have been free of disease for ≥ 3 years.
- c. No significant history of bleeding events or bleeding diathesis ≤ 6 months of registration unless the source of bleeding has been resected.
- d. No history of arterial thrombotic events, including, but not limited to, transient ischemic attack, cerebrovascular accident, unstable angina, angina requiring surgical or medical intervention, or myocardial infarction ≤ 6 months of registration.
- e. No history of clinically significant peripheral artery disease ≤ 6 months of registration.
- f. No history of uncontrolled congestive heart failure defined as NYHA Class III or greater.
- g. No history of gastrointestinal (GI) perforation ≤ 12 months of registration except for GI perforation related to a primary colorectal tumor that has since been fully resected.
- h. No history of malabsorption, uncontrolled vomiting or diarrhea, or any other disease significantly affecting GI function that could interfere with the absorption of oral agents.
- i. No history of allergic reaction attributed to compounds of similar chemical or biological composition to the study agents.

9. Comorbid Conditions

- a. No uncontrolled hypertension (defined as BP $> 160/90$).
- b. No serious or non-healing wound, ulcer, or bone fracture.
- c. No uncontrolled intercurrent illness, including, but not limited to, psychiatric illness/social situations that, in the opinion of the treating physician, may increase the risks associated with participation or treatment on the study or may interfere with the conduct of the study or interpretation of the study results.
- d. Patients positive for HIV are eligible only if they meet all of the following:
 - On effective anti-retroviral therapy
 - Undetectable HIV viral load by standard clinical assay ≤ 6 months of registration

- e. No known pre-existing hypercalcemia \leq 6 months of registration.
- f. No known active hyperparathyroid disease or other serious disturbance of calcium metabolism \leq 5 years of registration.
- g. No predisposing colonic or small bowel disorders in which symptoms are uncontrolled as indicated by $>$ 3 watery or soft stools daily in patients without a colostomy or ileostomy. Patients with a colostomy or ileostomy are allowed per treating physician discretion.
- h. No symptomatic genitourinary stones \leq 12 months of registration.
- i. Patients with treated brain metastases are eligible if follow-up imaging after CNS-directed therapy shows no evidence of progression \geq 28 days prior to registration.
- j. Patients with new or progressive brain metastases (active brain metastases) or leptomeningeal disease are eligible if the treating physician determines that immediate CNS-specific treatment is not required and is unlikely to be required during the first cycle of protocol-specified therapy after registration.
- k. No uncontrolled seizure disorders.
- l. No grade \geq 2 peripheral neuropathy, neurosensory toxicity, or neuromotor toxicity per CTCAE v5.0 regardless of causality.
- m. Patients must be able to swallow oral formulations of the agent.

10. Concomitant Medications

- a. Concurrent use of supplemental calcium and/or vitamin D is not permitted. Patients must discontinue the supplement(s) at least 7 days prior to registration. See Section 8.1.9 for more information.
- b. Concurrent use of thiazide diuretics (e.g. hydrochlorothiazide) is not permitted. Patients must discontinue the drug(s) or switch to an alternative anti-hypertensive agent at least 7 days prior to registration.
- c. Chronic concomitant treatment with oral corticosteroids, lithium, phenytoin, quinidine, isoniazid, and/or rifampin are not permitted. Patients must discontinue the agent(s) at least 7 days prior to registration. Short-term use of corticosteroids as antiemetic therapy is acceptable; see Section 8.1.10 for more information.
- d. Concurrent use of other anti-cancer therapy including chemotherapy, targeted, and/or biological agents is not permitted; see Section 8.1 for more information.

