ENROLLING: Phase 3 Clinical Trial for Patients With Previously Treated Metastatic Colorectal Cancer

PROCEADE
CRC-03 PHASE 3

Dear Healthcare Provider,

I am writing to inform you of a clinical study for adults with previously treated metastatic colorectal cancer (CRC), a patient population with limited treatment options. Outcomes continue to be poor for patients with metastatic CRC in third-line settings, who have been already exposed to irinotecan, oxaliplatin, 5-fluorouracil, and a vascular endothelial growth factor (VEGF) inhibitor.[1-3] Median overall survival with trifluoride/tipiracil (FTD-TPI) + bevacizumab, a commonly used regimen in the third-line setting, remains less than 1 year.[4]

Merck Healthcare KGaA is sponsoring a Phase 3 study of precemtabart tocentecan (Precem-TcT), an antibody-drug conjugate designed to deliver a payload of the topoisomerase 1 inhibitor exatecan into CEACAM5-expressing cancer cells. Study details can be found on the back of this letter.

CEACAM5 has limited expression in adult normal tissues, but is expressed at high levels in various adenocarcinomas, particularly in CRC. Single agent Precem-TcT has shown encouraging efficacy in patients with previously treated metastatic CRC. Precem-TcT, either as a single agent or in combination with bevacizumab, has demonstrated a toxicity profile that can be adequately managed with routine clinical supportive measures.[5-7]

Please consider discussing this study with your patients who may qualify. By referring patients, you are neither requiring them to participate nor guaranteeing their enrollment.

If you would like to refer a patient or request additional information, please contact:

Name:	**Site:**	**Email:**	**Phone number:**

Thank you in advance for your support of this important research.

1. Dasari A, Lonardi S, Garcia-Carbonero R, et al. *Lancet*. 2023;402(10395):41-53. 2. Mayer RJ, Van Cutsem E, Falcone A, et al. *N Engl J Med*. 2015;372(20):1909-19. 3. Grothey A, Van Cutsem E, Sobrero A, et al. *Lancet*. 2013;381(9863):303-12. 4. Prager GW, Taieb J, Fakih M, et al. *N Engl J Med*. 2023;388(18):1657-67. 5. Kopetz S, Boni V, Kato K, et al. *Nat Med*. 2025;31(10):3504-13. 6. Kopetz S, Garcia-Carbonero R, Han S-W et al. *J Clin Oncol* 2025:43:Suppl.16 Abstract 3038. 7. Kopetz S, Garcia-Carbonero R, Han S-W et al. *Ann Oncol*. 2025;36:Suppl 2:S600- S675. Abstract 962P.

Scan the code or visit PROCEADEcrc03study.com.

PIN: 9140

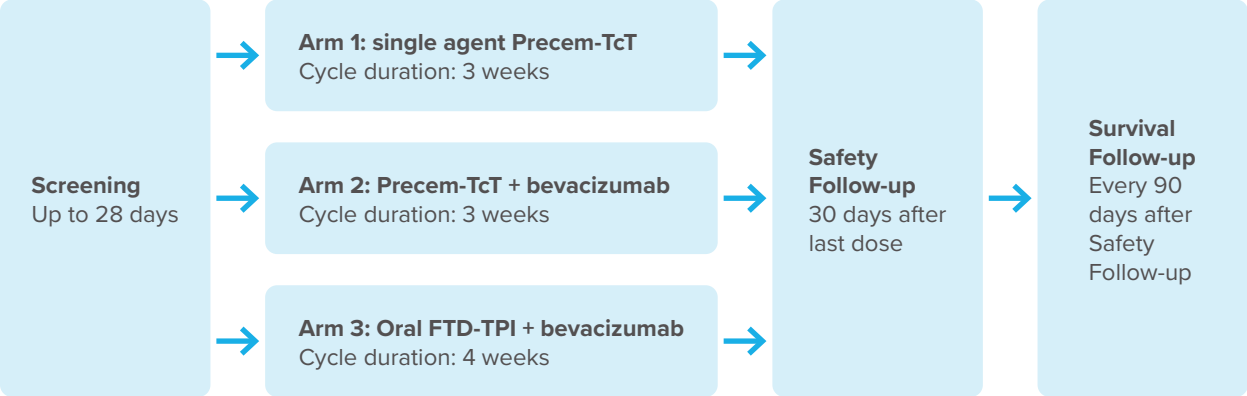
Phase 3 study of Precem-TcT +/- bevacizumab compared to FTP/TPI plus bevacizumab in participants with previously treated metastatic colorectal cancer

Primary Objective

To demonstrate improvement in overall survival with Precem-TcT as a single agent or in combination with bevacizumab compared to FTD-TPI plus bevacizumab

Study Design

Participants will be randomized in a 1:1:1 ratio to 1 of 3 open-label treatment groups. Treatment will continue until disease progression, death, unacceptable toxicity, withdrawal of consent, or any criterion for treatment discontinuation, whatever comes first.



Key Eligibility Criteria

Selected criteria are listed below. Other criteria apply.

Key inclusion criteria

- Age 18 or older at time of signing the Informed Consent Form
- Must have been previously exposed to a fluoropyrimidine, irinotecan, oxaliplatin, and bevacizumab
- Must have received and progressed on no more than 2 previous systemic treatment regimens in the metastatic setting
- Eastern Cooperative Oncology Group Performance Status 0 or 1
- Adequate hematologic, hepatic, and renal function
- Able to swallow oral tablets

Key exclusion criteria

- Adverse events from previous therapy not recovered to Grade 1 or less (exceptions apply)
- Malignancy within past 3 years (exceptions apply)
- Known brain metastases (exception: clinical stable without neurological symptoms)
- Contraindications to bevacizumab as described in its label
- Estimated life expectancy of < 4 months
- Congestive heart failure (New York Heart Association Class ≥ II), uncontrolled cardiac arrhythmia, unstable angina, myocardial infarction, coronary revascularization procedure, cerebral vascular accident, transient ischemic attack, thrombotic or hemorrhagic event, hemoptysis or any other significant cardiovascular condition or event within 180 days of randomization
- Active or prior interstitial lung disease/pneumonitis; History of idiopathic pulmonary fibrosis, obliterative bronchiolitis, or idiopathic pneumonitis

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