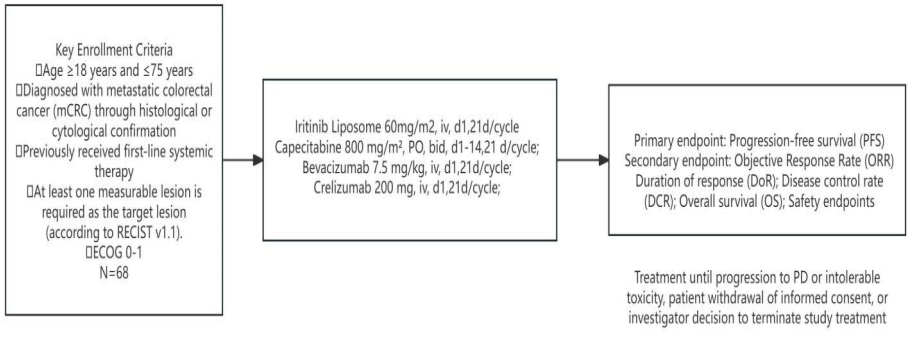
Essentials

Research Title	A single-arm, open-label clinical study of irinotecan liposome combined with capecitabine, bevacizumab, and camrelizumab as second-line or later treatment for patients with metastatic rectal carcinoma
Version and Date	V1.1 October 10,2025
Principal Investigator	Li Dezhi
Clinical TRIAL LEADERS Unit	The Fourth Affiliated Hospital of Zhejiang University School of Medicine
Research type	Prospective, single-arm clinical study
Indication	Metastatic rectal carcinoma
Planning study period	3 years
Subject investigated	Diagnosed as metastatic rectal carcinoma by histology or cytology
Purpose of research	Primary research objectives: Progression-free survival (PFS) assessed by the investigators Secondary objectives: 1) The objective response rate (ORR), duration of response (DoR), disease control rate (DCR), and overall survival (OS) assessed by the investigators; 2) Evaluate the safety of irinotecan liposome combined with capecitabine, bevacizumab, and camrelizumab for second-line and above treatment of metastatic colorectal carcinoma patients;
Planned enrollment	68 Example
Research design	Prospective, single-arm study 

Enrollment Criteria	1. Patients with a pathological diagnosis of rectal carcinoma; 2. They have received systematic treatment on the front line; 3. 18-75 years of age, male and female; 4. There must be at least one measurable lesion as the target lesion (according to RECIST v1.1 criteria); 5. ECOG：0 ~ 1； 6. expected survival ≥3 months; 7. Women of childbearing age must have a negative blood pregnancy test within 3 days prior to randomization and be willing to use appropriate contraceptive methods during the trial and for 6 months after treatment. For men, consent must be obtained to use appropriate contraceptive methods during the study and for 3 months after treatment. 8. All participants voluntarily enrolled in this study and signed the informed consent form.
Exclusion criteria	1. Patients with both RAS and BRAF wild-type mutations and left-sided primary colorectal tumors who have not received cetuximab in first-line therapy 2. patients with advanced rectal carcinoma who have MSI-H or dMMR 3. For patients with a history of other malignant diseases in the past 5 years, cured skin cancer and in situ cancer of cervix are excluded. 4. For patients with uncontrolled epilepsy, disorder central nervous system, or a history of mental disorders, the investigator may determine that their clinical severity could hinder the signing of an informed consent form or affect the patient's adherence to oral medication. 5. Clinically severe (i.e., active) heart disease, such as symptomatic coronary artery disease, congestive cardiac failure of NYHA class II or worse, or severe arrhythmias requiring pharmacological intervention (see Appendix 12), or a history of infarct myocardial within the past 12 months. 6. Organ transplant recipients requiring immunosuppression therapy 7. Severe, uncontrolled recurrent infections, or other severe, uncontrolled comorbidities 8. The baseline blood routine and biochemical indicators of the subjects did not meet the following criteria: hemoglobin ≥ 90g/L; absolute neutrophil count (ANC) ≥ 1.5 × 109/L; platelet count ≥ 100 × 109/L; ALT, AST ≤ 2.5 times the upper limit of normal; ALP ≤ 2.5 times the upper limit of normal; serum total bilirubin <1.5 times the upper limit of normal; serum creatinine <1 times the upper limit of normal; serum albumin ≥ 30g/L. 9. Known to have a deficiency in dihydropyridine dehydrogenase (DPD) 10. Allergy to any of the investigational drug components (e.g., irinotecan, irinotecan liposome, capecitabine, bevacizumab, or camrelizumab) 11. pregnant or lactating women

	12. received any of the following treatments: ● Concomitant medications within the first 2 weeks of randomization contained strong inhibitors/strong inducers of CYP3A4 or CYP2C8, or strong inhibitors of UGT1A1. ● Use of immunosuppressants or systemic hormone therapy for the purpose of immunosuppression within the first 2 weeks (dose>10mg/day of prednisone or other equivalent therapeutic hormones); ● received radiotherapy within the first 2 weeks of randomization; ● Surgery (e.g. thoracotomy, laparotomy) in the first 4 weeks of randomization; ● Received any other investigational drug in the previous 4 weeks, except for observational (non-interventional) clinical studies or intervention clinical study follow-up. 13. Coagulation dysfunction, having haemorrhagic diathesis or undergoing thrombolytic or anticoagulant therapy. The prophylactic use of low-dose aspirin (≤100mg/day) and low-molecular-weight heparin (enoxaparin 40mg/day and other low-molecular-weight heparins at equivalent doses) is permitted.
Administration method	➢ Iritinib liposome: 60 mg/m², administered via intravenous infusion, with the infusion completed within 90 minutes (±5 minutes). Administration is scheduled on day 1, once every 3 weeks. ➢ Capecitabine: 800 mg/m2, orally, twice daily, for days 1 to 14, repeated every 3 weeks. ➢ Bevacizumab: 7.5 mg/kg, intravenous infusion, on day 1, administered every 3 weeks; ➢ Crelizumab: 200 mg, intravenous infusion, on day 1, administered every 3 weeks
Therapeutic evaluation	RECIST1.1 was used.
Safety evaluation	NCI CTCAE 5.0 was used.
Evaluating indicator	Life signs, blood, urine, stool routine tests, blood biochemistry, electrocardiogram, echocardiography, observation of chemotherapy toxicity reactions, etc.
Subgroup analysis	PD-1 immunological detection stratification
Sample size calculation	The progression-free survival (PFS, Recist v1.1) of patients with metastatic rectal carcinoma treated with irinotecan liposome combined with capecitabine, bevacizumab, and camrelizumab in second-line or later therapy was improved from 5.7 months in previous studies to 8.3 months, α=0.05.

	With a power of 0.80,62 samples are required, and considering a 10% attrition rate, 68 participants are planned to be enrolled. This study is an exploratory study aimed at preliminarily evaluating the progression-free survival (PFS, Recist v1.1) of patients with metastatic rectal carcinoma treated with irinotecan liposome combined with capecitabine, bevacizumab, and camrelizumab as second-line or later therapy, without formal statistical assumptions. Statistical tests were not powered (Power) calculated or adjusted for multiplicity. All P-values for statistical tests were two-sided, with nominal P values.
Research progress	The first subject is expected to be enrolled in November 2025. The estimated enrollment date for the last subject is November 2027. The study is expected to conclude in November 2028.