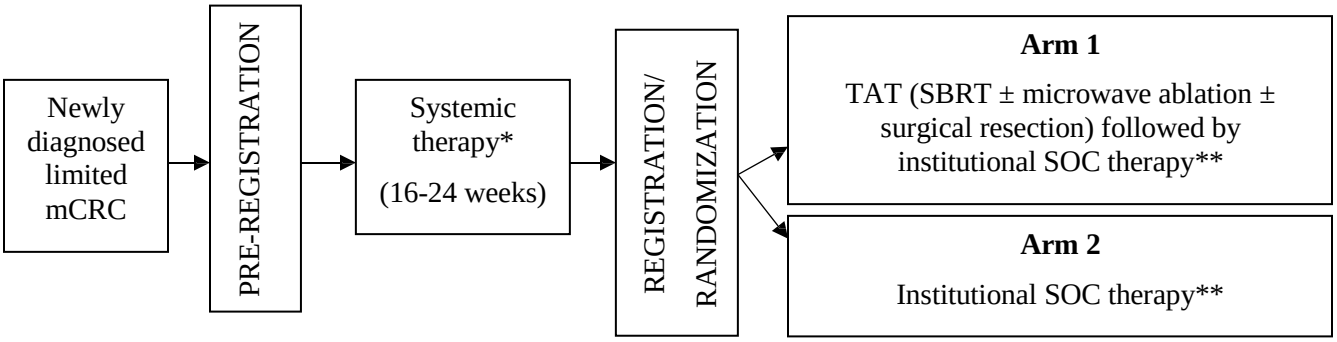
Alliance A022101 Schema

For 5FU-based chemotherapy: One Cycle = 14 Days

For capecitabine-based chemotherapy: One Cycle = 14 or 21 Days

For TAT regimen: One Cycle = 90 days



*Type of therapy will be determined by the treating physician. Up to 16 weeks (4 months) of systemic therapy may be administered prior to pre-registration. A minimum of 16 weeks of systemic therapy are required prior to registration, with a maximum of 24 weeks of total systemic therapy permitted prior to registration.
**Institutional standard of care (SOC) therapy may include additional systemic therapy as well as maintenance chemotherapy or treatment pause as determined by the treating physician.

All institutional SOC therapy (systemic, maintenance, treatment pause or restart, etc.) that occurs prior to disease progression will be deemed on-protocol treatment. Patients will be followed for 5 years or until death, whichever comes first.

Please refer to the full protocol text for a complete description of the eligibility criteria and treatment plan.

All sites must fulfill radiotherapy credentialing requirements. Refer to Section 15.0 of the protocol for full description of requirements.

Surgery, microwave ablation, and radiation therapy will be conducted at the registering institution. Chemotherapy may be administered at a non-registering institution. If the Group credited for enrollment is a non-Alliance Group, then other requirements from the credited Group may apply.

3.1 PATIENT SELECTION

For questions regarding eligibility criteria, see the Study Resources page. Please note that the Study Chair cannot grant waivers to eligibility requirements.

3.2 On-Study Guidelines

This clinical trial can fulfill its objectives only if patients appropriate for this trial are enrolled. All relevant medical and other considerations should be taken into account when deciding whether this protocol is appropriate for a particular patient. Physicians should consider the risks and benefits of any therapy, and therefore only enroll patients for whom this treatment is appropriate.

Clinicians should consider whether any conditions would make this protocol unreasonably hazardous for the patient.

In addition:

- Women and men of reproductive potential should agree to use an appropriate method of birth control throughout their participation in this study due to the teratogenic potential of the therapy utilized in this trial. Appropriate methods of birth control include abstinence, oral contraceptives, implantable hormonal contraceptives or double barrier method (diaphragm plus condom).

3.3 Pre-Registration Eligibility Criteria (Step 0)

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

3.2.1 Documentation of Disease

Histology/Pathology:

Histologically-confirmed metastatic colorectal adenocarcinoma.

No known microsatellite instable (MSI) tumor.

No known BRAF V600E mutation.

Disease Location/Sites:

Patients with treated brain metastases are eligible if follow-up brain imaging after CNS-directed therapy shows no evidence of progression. No known peritoneal and/or omental metastases. If radiologic studies suggest the presence of peritoneal disease, a diagnostic laparoscopy is recommended to verify the absence of peritoneal implants.

Primary tumor is already resected OR primary tumor is surgically amenable to resection, as determined by consultation and documentation with surgeon or documentation of discussion in the institutional multi-disciplinary tumor board where a surgeon confirms resectability. Patients with unresectable primary tumors are not eligible.

Four (4) or fewer apparent sites* of metastatic disease based on review by local medical team of baseline radiographic imaging obtained prior to initiation of systemic therapy.

- Sites of metastatic disease must be radiographically evident, but pathologic confirmation is not required.
- Liver-only metastatic disease is NOT permitted. For patients with liver metastases, there must be at least one other site of metastasis in addition to the liver to be eligible for this study.
- Metastatic lesions must be amenable to any combination of surgical resection, microwave ablation, and/or SABR. SABR is required for at least one lesion. Therefore, the patient must be seen by a radiation oncologist in consultation to verify eligibility.

*Single sites include:

- Each hemiliver (right and left), each lobe of the lungs, each adrenal gland, lymph nodes amenable to a single resection or treatment in a single SABR field, bone metastases amenable to treatment in a single SABR field.

3.2.2 Measurable Disease

Patients must have measurable disease per RECIST v1.1 (see Section 11.0).

3.2.3 Prior Treatment

A maximum of 16 weeks (4 months) of systemic therapy may be administered prior to pre-registration.

3.4 Registration Eligibility Criteria (Step 1)

Patients with known history or current symptoms of cardiac disease, or history of treatment with cardiotoxic agents, should have a clinical risk assessment of cardiac function using the New York Heart Association Functional Classification. To be eligible for this trial, patients should be class 2B or better.

Patients with a prior or concurrent malignancy whose natural history or treatment does not have the potential to interfere with the safety or efficacy assessment of the investigational regimen are eligible for this trial.

Use the spaces provided to confirm a patient's eligibility by indicating Yes or No as appropriate. It is not required to complete or submit the following page(s).

When calculating days of tests and measurements, the day a test or measurement is done is considered Day 0. Therefore, if a test were done on a Monday, the Monday one week later would be considered Day 7.

A female of childbearing potential is a sexually mature female who: 1) has not undergone a hysterectomy or bilateral oophorectomy; or 2) has not been naturally postmenopausal for at least 12 consecutive months (i.e., has had menses at any time in the preceding 12 consecutive months).

3.3.1 Disease Status

Patients must have no overt evidence of disease progression during systemic therapy prior to registration (see Section 11.0).

Not eligible for hepatic artery infusion pump (HAIP) therapy or benefit of HAIP therapy is undefined.

3.3.2 Measurable Disease

Patients must have measurable disease per RECIST v1.1 (see Section 11.0).

3.3.3 Prior Treatment

Patients must be receiving (or have received) first-line systemic therapy for metastatic disease for a minimum of 16 weeks (4 months) and a maximum of 24 weeks (6 months).

Prior definitive therapy, including adjuvant chemotherapy, must have been completed at least 12 months prior to diagnosis of metastatic disease.

3.3.4 Not pregnant and not nursing, because this study involves an agent or treatment that has known genotoxic, mutagenic, and teratogenic effects.

Therefore, for women of childbearing potential only, a negative pregnancy test done ≤ 14 days prior to registration is required.

3.3.5 Age ≥ 18 years

3.3.6 ECOG Performance Status: 0-2

3.3.7 Required Initial Laboratory Values:

Absolute Neutrophil Count (ANC)	≥ 1,500/mm^3
Platelet Count	≥ 50,000/mm^3
Creatinine	≤ 1.5 x upper limit of normal (ULN)
OR	
Calc. Creatinine Clearance	≥ 30 mL/min*
Total Bilirubin	≤ 1.5 x ULN
AST(SGOT) / ALT(SGPT)	≤ 3.0 x ULN**

* Calculated using the Cockcroft-Gault equation

** In the event of metastatic liver disease, ≤ 5 x ULN

3.3.8 Comorbid Conditions

HIV-infected patients on effective anti-retroviral therapy with undetectable viral load within 6 months are eligible for this trial. Note: HIV testing is not required for eligibility.

3.3.9 Concomitant Medications

No other planned concurrent investigational agents while on study.