Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Rationale

The ability of immunotherapy to unleash a patient's own T cells to kill MSI-H tumor cells is expected to occur in the adjuvant setting, and may result in reduced recurrence and improved patient survival. The rationale for combination of FOLFOX and atezolizumab is based upon the fact that FOLFOX is standard of care as adjuvant therapy for stage III colon cancer and promising data for combining chemotherapy with tezolizumab, including suggestion of immune priming. Since FOLFOX is standard adjuvant chemotherapy for stage III disease, it serves as the control arm for studies aiming to further improve patient outcomes. Atezolizumab will be continued as monotherapy for an additional 6 months following completion of FOLFOX for 6 months (12 cycles). The rationale for this approach is late and sustained responders with the use of pembrolizumab in metastatic MSI-H CRC, the importance of a definitive study, and alignment with ongoing/planned adjuvant studies using atezolizumab in other malignancies. Furthermore, sustained stimulation of the immune system may be key for long-term benefit with immunotherapy. There is a precedent with the anti-CTLA-4 antibody, ipilimumab, that is approved for the adjuvant therapy of melanoma with treatment duration up to 3 years. This study is intended to be definitive, and to have the potential to be practice-changing.

Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

Please use the headings above to navigate through the different sections of the poster

Objective

Primary

- To determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve DFS compared to FOLFOX alone in patients with stage III colon cancers and dMMR.

Secondary

- To determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve overall survival compared to FOLFOX alone in patients with stage III colon cancers and dMMR.
- To assess the adverse events (AE) profile and safety of each treatment arm, using the CTCAE and PRO-CTCAE.

Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

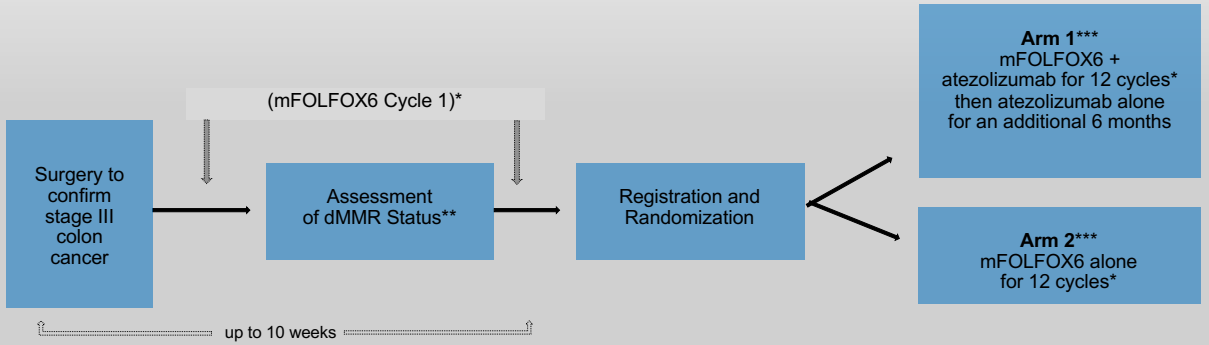
Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Study Schema



Please use the headings above to navigate through the different sections of the poster

* 1 cycle = 14 days. One cycle of mFOLFOX6 is allowed prior to registration. If Cycle 1 is started prior to registration, then the first post-registration cycle will be mFOLFOX6 Cycle 2. For patients who started Cycle 1 prior to registration and who are randomized to Arm 1, atezolizumab will start with Cycle 2.

** Assessment of dMMR status may be performed locally or at a reference laboratory. Retrospective central confirmation of dMMR testing is required for all patients. See Section 6.2.2 for specimen submission requirements and instructions.

*** The standard of care for the time window between the end of mFOLFOX6 Cycle 1 and the start of mFOLFOX6 Cycle 2 is 14 days; however, up to 28 days are allowed between the end of Cycle 1 and the start of Cycle 2 if delays are made due to toxicity.

Patients will be followed for recurrence every 6 months for two years after registration, and then annually for an additional 3 years. Patients will be followed for survival every 6 months for 8 years after registration.

Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Treatment Plan

Arm 1: mFOLFOX6 Plus Atezolizumab

Agent	Dose	Days	Cycle
Atezolizumab	840 mg	Day 1	Every 14 days
Oxaliplatin	85 mg/m^2	Day 1	Every 14 days
Leucovorin*	400 mg.m^2	Day 1	Every 14 days
Fluorouracil	400 mg/m^2 + 2400 mg/m^2	Day 1 + Day 1-3	Every 14 days

* Alternatively, leucovorin may be administered (via separate infusion containers) concurrently with oxaliplatin. Patients should receive 12 cycles of mFOLFOX6, including the cycle that may have been received prior to registration. Patients should receive 12 months (25 cycles) of atezolizumab, starting on Day 1 Cycle 1 of mFOLFOX6.

Arm 2: mFOLFOX6

Agent	Dose	Days	Cycle
Oxaliplatin	85 mg/m^2	Day 1	Every 14 days
Leucovorin*	400 mg.m^2	Day 1	Every 14 days
Fluorouracil	400 mg/m^2 + 2400 mg.m^2	Day 1 + Day 1-3	Every 14 days

* Alternatively, leucovorin may be administered (via separate infusion containers) concurrently with oxaliplatin. Patients should receive 12 cycles of mFOLFOX6, including the cycle that may have been received prior to registration.

Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY

NCI National Clinical Trials Network
a National Cancer Institute program

Please use the headings above to navigate through the different sections of the poster

Key Eligibility Criteria

- Histologically proven stage III colon adenocarcinoma (any T [Tx, T1, T2, T3, or T4], N1-2M0; includes N1C). Presence of deficient (d) DNA mismatch repair (dMMR). MMR status must be assessed by immunohistochemistry (IHC) for MMR protein expression (MLH1, MSH2, MSH6, PMS2) where loss of one or more proteins indicates dMMR. dMMR may be determined either locally or by site-selected reference lab.
- Tumors must have been completely resected.
- No prior medical therapy (chemotherapy, immunotherapy, biologic or targeted therapy) or radiation therapy for colon cancer except for one cycle of mFOLFOX6.
- Age ≥ 18 years
- ECOG Performance Status ≤ 2
- Not Pregnant and Not Nursing
- Specific required initial lab values *(see protocol)*
- No active known autoimmune disease, including colitis, inflammatory bowel disease (i.e. ulcerative colitis or Crohn's disease), rheumatoid arthritis, panhypopituitarism, adrenal insufficiency.
- No other planned concurrent investigational agents or other tumor directed therapy (chemotherapy, radiation) while on study. No systemic daily treatment with either corticosteroids (>10 mg daily prednisone equivalents) or other immuno-suppressive medications within 7 days of registration.
- No known history of severe allergic anaphylactic reactions to chimeric, human or humanized antibodies, or fusion proteins. No known hypersensitivity to CHO cell products or any component of the atezo-lizumab formulation. No known allergy to 5-fluorouracil, oxaliplatin, or leucovorin.

Alliance A021502: Randomized Trial of Standard Chemotherapy Alone or Combined with Atezolizumab as Adjuvant Therapy for Patients with Stage III Colon Cancer and Deficient DNA Mismatch Repair (ATOMIC: Adjuvant Trial of Deficient Mismatch Repair in Colon Cancer)

Frank A. Sinicrope, MD, Walter Peters, MD, Kabir Mody, MD

Mayo Clinic and Baylor University Medical Center

TAP TO RETURN TO KIOSK MENU

Funding Support

Alliance A021502 is funded by the National Institutes of Health through National Cancer Institute grant awards, and in part by the Genentech, Inc.

Please use the headings above to navigate through the different sections of the poster

Contact Us

Study Chair: Frank A. Sinicrope, MD
E-mail: sinicrope.frank@mayo.edu
Phone: 507-266-5365

Study Chair: Walter Peters, MD
E-mail: walter.peters@baylorhealth.edu
Phone: 469-800-7600

Kabir Mody, MD
E-mail: mody.kabir@mayo.edu
Phone: 904-953-2795

Protocol Coordinator: Alexandra LeVasseur
E-mail: alevasseur@uchicago.edu