



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)

Frank Sinicrope, MD, Study Chair

Informational Webinar, September 30, 2020

Presentation Objectives

- Protocol Overview
 - Study Design, Eligibility Criteria, Study Calendar
 - Update #06 Changes
- Updated Funding Overview
 - Revised Funding Sheet
- General Reminders



Alliance A021502 Protocol Overview

Frank Sinicrope, MD
A021502 Study Chair

Informational Webinar, September 30, 2020

Presentation Overview

- Study Design
- Treatment Plan
- Eligibility Criteria
- Study Calendar
- Specimen Submission
- Update #06 Changes

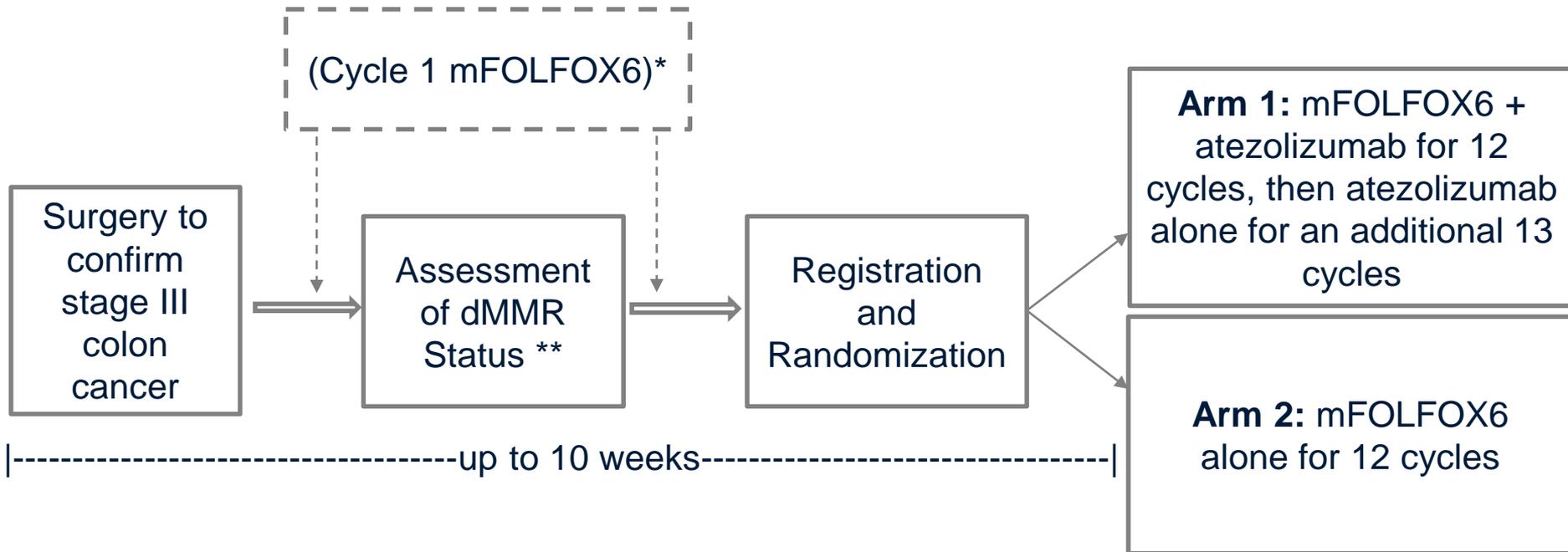
Study Design

- Primary Objective:
 - To determine whether atezolizumab combined with FOLFOX and its continuation as monotherapy can significantly improve disease-free survival (DFS) compared to FOLFOX alone in patients with stage III colon cancers and dMMR.

Study Design (continued)

- Accrual Goal = 700 patients
 - Current accrual = 342 patients (as of 09/29/2020)
- Patients will be followed for recurrence and survival every 6 months for the first 2 years after registration, then for recurrence annually for years 3-5 after registration, and then survival every 6 months for years 3-8 after registration.

Study Design (continued)



* One cycle of mFOLFOX6 is allowed prior to registration

** dMMR status assessed via local or reference lab testing of MMR by IHC.

Treatment Plan

- Administration Schedule:
 - Atezolizumab 840 mg IV Day 1 (Arm 1 patients only)
 - Oxaliplatin 85 mg/m² IV on Day 1
 - Leucovorin 400 mg/m² IV on Day 1
 - Fluorouracil 400 mg/m² IV bolus on Day 1 + 2400 mg/m² IV on Days 1-3
- Administration of one cycle of mFOLFOX6 prior to registration is permitted.
 - Treatment must be administered at registering institution.
 - Doses received must follow those listed above.
 - Patients who receive Cycle 1 of mFOLFOX6 prior to registration and who are randomized to Arm 1 will begin atezolizumab with Cycle 2 of mFOLFOX6.

Treatment Plan (continued)

- Treatment is to begin within 14 days of registration.
 - Cycle 1 of mFOLFOX6 must begin within 10 weeks of surgery.
 - Best practice is 3-6 weeks between surgery and C1 of chemo.
- One cycle is defined as 14 days of treatment.
 - SOC window between end of C1 and start of C2 is 14 days.
 - Up to 28 days are allowed if delays occur due to toxicity.
- Chemotherapy and immunotherapy must be administered at the registering institution.

Eligibility Criteria

- Histologically proven stage III colon adenocarcinoma.
 - Any T, N₁₋₂M0 (includes N1C)
- Presence of deficient MMR (dMMR) via IHC.
 - Loss of MLH1, MSH2, MSH6, or PMS2.
 - MMR testing may be done locally or at a site-selected reference laboratory.
 - Patients with known Lynch Syndrome are allowed.
- Tumor(s) must have been completely resected.
 - Entire tumor must have resided in colon (i.e. rectal involvement is an exclusion).
 - No evidence of residual involved lymph node disease or metastatic disease at registration.

Eligibility Criteria (continued)

- No prior chemotherapy or radiation for colon cancer.
 - (Other than one cycle of mFOLFOX6 prior to registration)
- No active autoimmune disease.
- No known active hepatitis B or C.
- No active pulmonary disease with hypoxia.
- No grade ≥ 2 peripheral motor or sensory neuropathy.
- HIV positive patients are allowed.
- No other planned concurrent investigational agents or other tumor directed therapy.
- No systemic daily corticosteroids or other immunosuppressive medications within 7 days.

Eligibility Criteria (continued)

- No known allergies to any of the study drugs.
- Not pregnant and not nursing.
 - Negative pregnancy test required ≤ 7 days prior to registration
- Age ≥ 18 years
- ECOG Performance Status ≤ 2
- All required initial laboratory study results are within the ranges specified in Section 3.2.7 of the protocol.

Study Calendar

Footnotes in column headings (e.g. *, **, ***) pertain to the entire column and provide additional information about the specific time point.

Footnotes in boxes (e.g. 1, 2, etc.) provide additional information about the specific test, study, etc.

Footnotes in boxes (e.g. A, B, C, D) pertain only to the corresponding item at that specific time point.

	Prior to Registration*	Arm 1: Day 1 of each cycle*	Arm 2: Day 1 of each cycle*	End of treatment follow-up**	Post-treatment follow-up ***
Tests & Observations					
History and Physical, Weight, PS	A	A	A	X	X
Height	X				
Pulse, Blood Pressure	X	X	X	X	
O ₂ Saturation	X(1)	X(1)		X(1)	
CTCAE Adverse Event Assessment		X(2)	X(2)	X(2)	X(2)
PRO-CTCAE Adverse Event Assessment	X(3)	X(3)	X(3)	X(3)	
Registration Fatigue/ Uniscale Assessment	X(4)				
Colonoscopy	B				B
Laboratory Studies					
Complete Blood Count, incl. Diff.	X	X	X	X	
Chemistry	X(5)	X(5)	X(5)	X(5)	
TSH	X(6)	X(6)			
Hep B Surface Ag & Hep C ab (Physician Discretion)	X				
Urinalysis	X(7)	X(7)			
Serum or Urine HCG	X(8)				
CEA	X(9)	X(9)	X(9)		X(9)
CD4 Count & Viral Load	X(10)				
dMMR Testing	X				
Staging					
CT of Chest/Abd/Pelvis or MRI of Chest/Abd/Pelvis	C	D	D	D	D

Study Calendar (continued)

- In general, the following items are required on Day 1 of each cycle for both Arm 1 and Arm 2 patients:
 - H&P, pulse, blood pressure, CTCAE, PRO-CTCAE, complete blood count incl. differential, and chemistry panel.
 - For Arm 1 Patients Only: O₂ saturation, TSH, and urinalysis are also required at varying intervals per Section 5.0.
- CT (or MRI) is required every 6 months for the first 2 years after registration, then annually for years 3-5 after registration or until evidence of relapse, whichever comes first.
 - Imaging modality used at baseline must be used for all subsequent imaging time points.

Specimen Submission

Specimen Submission Schedule for the Alliance A021502 Study					
	Prior to treatment	4 weeks after initiation of treatment	4.5 months after initiation of treatment	6 months after end of adjuvant therapy	Time of recurrence
Mandatory Submissions for <u>All Patients</u> Registered to the A021502 Main Study:					
10 Superfrost® Plus Micro Slides	X				
H&E slide <u>AND</u> FFPE tumor block	X				
FFPE normal block	X				
For Patients Registered to A021502-ST1 and/or A021502-PP1, Submit the Following:					
FFPE tumor block	X				X
EDTA platelet poor plasma & buffy coats	3 x 10 mL		3 x 10 mL	3 x 10 mL	3 x 10 mL
Whole blood	3 x 8.5 mL	3 x 8.5 mL	3 x 8.5 mL	3 x 8.5 mL	
Stool	3 x 25 mL		3 x 25 mL	3 x 25 mL	

Mandatory submission of 10 Superfrost® Plus Micro Slides (or alternatives) to the central laboratory, HistoGeneX, not the Alliance Biorepository.

There are **three** different blood kits and one stool kit which correspond to various time points. Kit ordering instructions can be found in the A021502 Correlative Science Manual.

All specimen processing, storing, and shipment information can be found in the A021502 Correlative Science Manual on Alliance and CTSU websites.

Major Update #06 Changes

- Eligibility Criteria (Section 3.2)
 - Description of disease status updated to address patients with *multiple* primary colon cancers.
 - “Patients with more than one primary colon adenocarcinoma are eligible if the qualifying stage III tumor is confined to the colon, and not rectum, and the other cancers of lower stage are removed in the en bloc R0 resection.”
- Study Calendar (Section 5.0)
 - References to Footnotes 1-10 moved from just first column to now all applicable time point columns.
 - A +/- 1 month window added for follow-up time points.
 - Bicarbonate *or total* CO₂ now allowed.

Major Update #06 Changes

- Alliance Policy Concerning Use of Growth Factors (Section 8.1.8)
 - Description of growth factor use updated to align with current ASCO Guidelines.
 - “Blood products and growth factors should be utilized at the discretion of the treating physician as clinically warranted and following institutional policies and recommendations.”



Alliance A021502 Updated Funding Overview

Alexandra LeVasseur
A021502 Protocol Coordinator

Informational Webinar, September 30, 2020

Updated Funding Information

- Revised Funding Sheet
 - Sites will receive an additional \$1,000 per-case payment for enrollments to Alliance A021502 in recognition of increased effort necessitated by this registration NDA trial.
 - Non-federal payment for patient enrollment increased from \$3,500 to \$4,500.
 - Increased per-case payment *will also be applied retrospectively* for patients enrolled to the trial prior to the funding sheet update.
 - Retrospective payments will be disbursed after the new year.
 - Revised Funding Sheet is posted to Alliance and CTSU websites.
 - Questions concerning the Funding Sheet should be directed to John Taylor (jtaylor3@bsd.uchicago.edu).



Alliance A021502 General Study Reminders

Alexandra LeVasseur
A021502 Protocol Coordinator

Informational Webinar, September 30, 2020

General Reminders

- Patient-completed Booklet Requests
 - Requests are to be made by completing the most current CTSU Supply Request Form and submitting via the CTSU Regulatory Portal, not by fax; see Section 4.3.
- Mandatory Tissue Submission
 - Tissue for central dMMR confirmation testing must be submitted directly to the central laboratory, HistoGeneX.
 - Address for HistoGeneX can be found at the top of the A021502 Requisition Form on Alliance and CTSU websites.
 - Tumor tissue and normal tissue blocks must be submitted directly to the Alliance Biorepository at Mayo Clinic.

General Reminders (cont.)

- Data Completion Guideline (DCG)
 - Updated DCG will be posted 10/15 that includes guidance on the follow-up periods.
- Delegation of Tasks Log (DTL)
 - Please keep DTLs up to date in real time to include staff comings and goings.
- Protocol Deviation (PD)
 - Please ensure PDs and appropriate CAPAs are being reported via Rave (if required).
 - If there is a PD for COVID-19 mitigation to be reported, please do so in the COVID-19 Data Base in Rave.

Q&A

Presentation materials will be posted to the Alliance and CTSU websites.

**THANK YOU FOR YOUR
PARTICIPATION!**