

**ALLIANCE FOR CLINICAL TRIALS IN ONCOLOGY**

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**PROTOCOL UPDATE TO ALLIANCE A021502**

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**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**

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|---|---|
| <input checked="" type="checkbox"/> <b>Update:</b>  | <input type="checkbox"/> <b>Status Change:</b>          |
| <input type="checkbox"/> Eligibility changes  | <input type="checkbox"/> Activation                     |
| <input checked="" type="checkbox"/> Therapy / Dose Modifications / Study Calendar changes | <input type="checkbox"/> Closure                        |
| <input checked="" type="checkbox"/> Informed Consent changes                              | <input type="checkbox"/> Suspension / temporary closure |
| <input checked="" type="checkbox"/> Scientific / Statistical Considerations changes       | <input type="checkbox"/> Reactivation                   |
| <input checked="" type="checkbox"/> Data Submission / Forms changes                       |   |
| <input checked="" type="checkbox"/> Editorial / Administrative changes                    |   |
| <input checked="" type="checkbox"/> Other: Added CTSU Delegation of Task Log              |   |

*Expedited review is allowed. IRB approval (or disapproval) is required within 90 days. Please follow your IRB of record guidelines.*

**UPDATES TO THE PROTOCOL:**

**Cover Page**

- Tyler Zemla has replaced Dr. Qian Shi as the Secondary Statistician, and all contact information has been updated accordingly.
- The title for Dr. Amylou Dueck has been updated to now read: “Health Outcomes Committee Co-Chair and Statistician” (previously, “Health Outcomes Statistician”).

**Schema**

- In footnote \*, the phrase “of mFOLFOX6” has been added to the 3<sup>rd</sup> sentence for clarity.
- In footnote \*, the following modifications have been made in the 4<sup>th</sup> sentence for clarity:
  - The phrase “received Cycle 1 of mFOLFOX6” has replaced “started Cycle 1.”
  - The phrase “of mFOLFOX6” has been added to the end of the sentence.
- In footnote \*\*, the phrases “for eligibility” and “site-selected” have been added to the 1<sup>st</sup> sentence for clarity.
- In footnote \*\*, the phrase “to gauge the false-positive rate in local testing (not for eligibility)” has been added to the end of the 2<sup>nd</sup> sentence for clarity.

- The 1<sup>st</sup> paragraph below the footnotes has been completely revised for clarity to now read: **“Patients will be followed for recurrence and survival every 6 months for the first two years after registration, then survival every 6 months and recurrence once annually for years 3-5 after registration, and then survival every 6 months for years 5-8 after registration”** (previously, **“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”**).

#### [Section 4.0 \(Patient Registration\)](#)

- [Section 4.1 \(CTEP Investigator Registration Procedures\)](#) and [Section 4.2 \(CTEP Associate Registration Procedures/CTEP-IAM Account\)](#) have been removed and replaced with a new [Section 4.1](#) entitled **“CTEP Registration Procedures”** which includes updated CTSU boilerplate language. Subsequent sections have been renumbered accordingly.
- All text in [Section 4.2 \(CTSU Registration Procedures\)](#) (formerly, [Section 4.3](#)) has been completely revised to include updated CTSU boilerplate language.
- A new subsection entitled **“Delegation of Task Log (DTL)”** has been added as [Section 4.2.5](#) to include current CTSU boilerplate language. Sites are expected to complete and submit the DTL along with the issuance of this update.
- All text in [Section 4.4 \(Patient Registration/Randomization Procedures\)](#) (formerly, [Section 4.5](#)) has been completely revised to include updated CTSU boilerplate language.

#### [Section 4.6 \(Stratification Factors and Treatment Assignments\)](#)

- The phrase **“and Treatment Assignments”** has been added to the section title for accuracy.
- A new 1<sup>st</sup> subsection heading entitled **“Permuted Block”** and a new 1<sup>st</sup> paragraph have been added before the bulleted list and a new 2<sup>nd</sup> paragraph has been added after the bulleted list in order to provide information on the method used to randomize patients to one of the two treatment arms.

#### [Section 5.0 \(Study Calendar\)](#)

- Footnote \*\*\* has been completely revised for clarity to now read: **“Patients will be followed for recurrence and survival every 6 months (+/- 1 month) for the first two years after registration, then survival every 6 months and recurrence once annually for years 3-5 after registration, and then survival every 6 months for years 5-8 after registration. Recurrence follow-up will continue per the schedule above for 5 years after registration or until evidence of relapse, whichever comes first. Survival follow-up will continue per the schedule above for 8 years after registration or until death, whichever comes first. See also Section 12.0”** (previously, **“Patients will be followed for recurrence every 6 months (+/- 1 month) for two years after registration, and then annually for an additional 3 years or until evidence of relapse, whichever comes first. Patients will be followed for survival every 6 months (+/- 1 month) for 8 years after registration or until death, whichever comes first. See also Section 12.0”**).
- In footnote 5, the word “serum” has been added before “creatinine” in the 1<sup>st</sup> sentence to specify that this value should be obtained via serum rather than plasma.
- In footnote D, a new 1<sup>st</sup> sentence has been added for clarity that reads: **“The same imaging modality used at baseline must be used for all subsequent scans.”**
- In the now 2<sup>nd</sup> sentence of footnote D, the phrase **“for the first 2 years after registration,”** has replaced **“from time of registration for 2 years”** and the phrase **“years 3-5 after registration”** has replaced **“an additional 3 years”** for clarity.

#### [Section 6.1 \(Data Collection and Submission\)](#)

All text in the 1<sup>st</sup> paragraph has been completely revised to include updated CTSU boilerplate language.

#### [Section 6.2 \(Specimen Collection and Submission\)](#)

In footnote 1, the phrase **“and within 30 days of registration”** has been added to the 3<sup>rd</sup> sentence for clarity.

### Section 6.2.2.1 (Superfrost® Plus Micro Slides Submission)

- A new 3<sup>rd</sup> sentence has been added to the 1<sup>st</sup> paragraph to clarify the slide processing requirements. It reads: “(Note: slides should not be paraffin dipped).”
- In the now 4<sup>th</sup> sentence of the 1<sup>st</sup> paragraph, the phrase “and within 30 days of registration” has been added for clarity.
- A new 3<sup>rd</sup> sentence has been added to the 4<sup>th</sup> paragraph to note that the results of the retrospective dMMR confirmation will not be shared with sites/patients, and the results of this confirmation are not used to determine eligibility.

### Section 7.0 (Treatment Plan/Intervention)

- In the 4<sup>th</sup> sentence of the 4<sup>th</sup> paragraph, the phrase “the local” has been added for clarity.
- In the 5<sup>th</sup> sentence of the 4<sup>th</sup> paragraph, “end of mFOLFOX6 Cycle 1” has been corrected to “start of mFOLFOX6 Cycle 1,” and “Day 1 of Cycle 1” has been corrected to “Day 14 of Cycle 1.”
- In the 5<sup>th</sup> sentence of the 6<sup>th</sup> paragraph and in the 5<sup>th</sup> and 7<sup>th</sup> sentences of the 7<sup>th</sup> paragraph, the word “should” has replaced “will” for accuracy and clarity.

### Section 7.1 (Arm 1: mFOLFOX6 Plus Atezolizumab)

- A new 1<sup>st</sup> paragraph has been added below the table for clarity that reads: “Atezolizumab should be the first drug administered for Cycle 1 as no premedication is allowed prior to the first dose of atezolizumab; see Section 7.0 and Section 8.1.4 for additional details.”
- The following language has been added to the end of the 2<sup>nd</sup> sentence of the now 2<sup>nd</sup> paragraph below the table for clarity: “patients who receive one cycle of mFOLFOX6 prior to registration should start atezolizumab on Day 1 Cycle 2 of mFOLFOX6.”

### Section 9.3.1 (Late Phase 2 and Phase 3 Studies: Expedited Reporting Requirements for Adverse Events that Occur on Studies Under an IND/IDE ≤ 30 Days of the Last Administration of the Investigational Agent/Intervention)

The following changes have been made within the “**Additional Instructions or Exclusions to CTEP-AERS Expedited Reporting Requirements for Phase 2 and 3 Trials Utilizing an Agent Under a CTEP IND or non-CTEP IND**” section for accuracy and clarity:

- In the subsection title, the word “**Exclusion**” has been corrected to “**Exclusions**.”
- In the 3<sup>rd</sup> bullet, the 1<sup>st</sup> sentence has been revised to now read “Grade 3 or 4 hematosuppression resulting in hospitalization does not require CTEP-AERS, but should be submitted as part of study results” (previously, “Grade 3/4 hematosuppression and hospitalization resulting from such do not require CTEP-AERS, but should be submitted as part of study results”). The 2<sup>nd</sup> sentence of the 3<sup>rd</sup> bullet has been completely removed as it had been included in error (previously, “All other grade 3, 4, or 5 adverse events that precipitate hospitalization or prolong an existing hospitalization must be reported via CTEP-AERS”).
- In the 5<sup>th</sup> bullet, the phrase “resulting in hospitalization does not” has replaced “and hospitalization resulting from such do not.”
- In the 6<sup>th</sup> bullet, the phrase “not resulting in hospitalization” has been added.
- In the 7<sup>th</sup> bullet, the phrase “oral mucositis resulting in hospitalization” has replaced “mucositis and hospitalization resulting from such.”
- In the 8<sup>th</sup> bullet, the phrase “oral mucositis not resulting in hospitalization” has replaced the word “mucositis.”
- In the 9<sup>th</sup> bullet, the phrase “peripheral sensory neuropathy resulting in hospitalization” has replaced “neuropathy and hospitalization resulting from such.”
- In the 10<sup>th</sup> bullet, the phrase “peripheral sensory neuropathy not resulting in hospitalization” has replaced the word “neuropathy.”

- In the 11<sup>th</sup> bullet, the phrase “resulting in hospitalization” has replaced “and hospitalization resulting from such.”
- In the 12<sup>th</sup> bullet, the phrase “not resulting in hospitalization” has been added.
- In the 13<sup>th</sup> bullet, the phrase “Grade 1-3 hypersensitivity reaction resulting in hospitalization” has replaced “Grade 1-4 hypersensitivity reaction and hospitalization resulting from such.”
- In the 14<sup>th</sup> bullet, the phrase “not resulting in hospitalization” has been added.
- In the 15<sup>th</sup> bullet, the phrase “resulting in hospitalization” has replaced “and hospitalization resulting from such.”
- In the 16<sup>th</sup> bullet, the phrase “not resulting in hospitalization” has been added.
- In the 17<sup>th</sup> bullet, the phrase “resulting in hospitalization” has replaced “and hospitalization resulting from such.”
- In the 18<sup>th</sup> bullet, the phrase “not resulting in hospitalization” has been added.

### Section 11.1 (Schedule of Evaluations)

In the 1<sup>st</sup> sentence of the 1<sup>st</sup> bullet under the 1<sup>st</sup> paragraph, the phrase “for the first 2 years after registration” has replaced “for 2 years” and the phrase “(i.e. years 3-5 after registration)” has been added to the end of the same sentence for clarity.

### Section 12.1 (Duration of Treatment)

- In the 1<sup>st</sup> sentence of the 1<sup>st</sup> paragraph, the phrase “6 months of atezolizumab alone” has replaced “6 months atezolizumab” for clarity.
- In the 2<sup>nd</sup> paragraph, the 3<sup>rd</sup> sentence has been replaced with new 3<sup>rd</sup> – 5<sup>th</sup> sentences for clarity that begin “Patients will be followed...,” “Recurrence follow-up...,” and “Survival follow-up...,” respectively (previously, “Patients will be followed for recurrence every 6 months (+/- 1 month) for two years after registration, and then annually for an additional 3 years or until evidence of relapse, whichever comes first”).
- The 3<sup>rd</sup> paragraph has been removed as this information has been revised and included in the new language in the 2<sup>nd</sup> paragraph for clarity (previously, “Patients will be followed for survival every 6 months (+/- 1 month) for 8 years after registration or until death, whichever comes first”).

### Section 13.6 (Protocol-specific Monitoring Plan)

- A new 1<sup>st</sup> paragraph has been added before the subsection headings for clarity that begins: “This trial will utilize both central and on-site monitoring....”
- The phrase “**and Source Data Verification**” has been added to the 1<sup>st</sup> subsection heading for clarity.
- All text previously included in the “**Central Data Monitoring and Source Data Verification**” section has been replaced with five new paragraphs and subsequent bullet points and list items in order to provide a more comprehensive summary of the centralized data monitoring plans.
- Under the “**On-site Monitoring**” heading, nine new paragraphs and subsequent bullet points have been added as new 1<sup>st</sup>-9<sup>th</sup> paragraphs in order to provide a more comprehensive summary of the on-site monitoring plans.

### Appendix I (Quality of Life Measures)

- A new 2<sup>nd</sup> page has been added within Appendix I before the FACT-C questionnaires in order to provide an example of the instructional cover page sheet that has been added as the new 1<sup>st</sup> page of the Patient QOL Booklets that are ordered through the CTSU.
- A new 9<sup>th</sup> page has been added within Appendix I before the PRO-CTCAE questionnaires in order to provide an example of the instructional cover page sheet that has been added as the new 1<sup>st</sup> page of the PRO-CTCAE Booklets that are ordered through the CTSU.
- In the 1<sup>st</sup> paragraph of the now 2<sup>nd</sup> page of the PRO-CTCAE Booklet example (i.e. the 10<sup>th</sup> page of Appendix I overall), an “X” has been added to the 2<sup>nd</sup> sentence as it had been erroneously omitted.

- A new 13<sup>th</sup> question has been added to the PRO-CTCAE Booklet example in order to assess a patient's hand-foot syndrome severity and to match the PRO-CTCAE Booklets that are ordered through the CTSU. Subsequent questions have been renumbered accordingly.
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## **UPDATES TO THE MODEL CONSENT:**

### **What exams, tests, and procedures are involved in this study?**

In the bulleted list below the 5<sup>th</sup> paragraph, the following corrections have been made:

- A new 2<sup>nd</sup> bullet has been added so as to state that the thyroid test performed prior to registration is not needed with the usual approach but will be required for all patients before registering on this study. It reads: "A thyroid test before you begin study treatment."
- In the now 4<sup>th</sup> bullet, the phrase "a thyroid test and" has been removed as the thyroid tests performed for Group 1 patients while on treatment are part of the usual care for atezolizumab, and this phrase had erroneously been included in this section.

### **What are the costs of taking part in this study?**

Under the "Costs Paid by the Study" heading, the following changes have been made for clarity:

- A new 1<sup>st</sup> paragraph has been added to clarify that the cost of the baseline thyroid test will be paid for by the study for all patients, not just patients in Group 2. It reads: "For patients in both Group 1 and Group 2, the thyroid test performed before you begin study treatment will be at no charge to you or your insurance company."
- In the 3<sup>rd</sup> sentence of the now 2<sup>nd</sup> paragraph, the phrase "thyroid and" has been removed as this monitoring is part of the usual care during treatment with atezolizumab, and therefore would be billed to the patient's insurance (or would be the patient's responsibility), and the word "your" has been corrected to "you" within the same sentence.

**A replacement protocol and consent document have been issued.**

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**ATTACH TO THE FRONT OF EVERY COPY OF THIS PROTOCOL**

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