Alliance for Clinical Trials in Oncology
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August 24, 2021

Dear Alliance A031501 Physician Participant:

This letter is to provide you with information regarding Alliance A031501, "Phase III randomized Adjuvant study of MK-3475 (peMBrolizumAb) in muScle invaSive and locAlly aDvanced urOthelial caRcinoma (AMBASSADOR) versus Observation."

The FDA recently approved nivolumab, a PD-1 inhibitor (similar to pembrolizumab), as adjuvant therapy for patients with urothelial carcinoma (UC) who are at high risk of recurrence after undergoing radical resection. All patients were treated within 120 days of radical resection of urothelial carcinoma of the bladder or upper urinary tract (renal pelvis or ureter). **Therefore, effective immediately, A031501 is permanently closed to new patient accrual.**

The following actions are now required:

1. Upon receipt of this notice, physicians (or nurse practitioners/physician assistants) should discuss the new approval of nivolumab with all patients enrolled in this trial (discussion over the phone or via telemedicine is acceptable). To facilitate this discussion, a sample patient letter is available on the Alliance A031501 study page on the member side of the Alliance and CTSU web sites. Documentation of the discussion with the patient should be kept in the patient's medical record.
2. Recommendations for patients currently enrolled on A031501 are as follows:
    a. Patients currently receiving active treatment can continue on therapy with pembrolizumab per the protocol-specified treatment plan, if after discussion, the patient and physician agree that this is the most appropriate medical intervention for the patient. Patients may switch to nivolumab therapy as another option if they are within 120 days of their radical resection. Nivolumab will not be covered by the study.
    b. For patients randomized to observation and within 120 days of radical resection, physicians should discuss the possibility of treating patients with nivolumab. A patient may continue on observation, if after discussion, the patient and physician agree that this is the most appropriate medical intervention for the patient.
    c. Patients who are no longer receiving protocol treatment should be informed of the FDA approval of nivolumab. Patients who have progressed, are lost to follow-up, or withdrew consent do not need to be informed of this FDA approval.

d. Patients who have consented and have not yet been pre-registered, or those who have pre-registered to A031501 and have not yet been randomized will not register to A031501.

3. Required testing, follow-up, and data submission will continue for all randomized patients according to the protocol.
4. The costs of the nivolumab will be covered by the patient/insurance. Nivolumab will not be provided by the A031501 study.
5. Please note that it is not necessary to obtain IRB approval before notifying patients. Investigators should, however, notify the IRB of Record for the study at their sites at this time, and provide copies of the physician and patient letters. If the NCI CIRB is the IRB of Record at an investigator's site, the Alliance will inform the NCI CIRB of this notification and provide copies of the physician and patient letters to the NCI CIRB.

Questions regarding the management of individual patients on protocol therapy can be directed to Dr. Andrea Apolo at andrea.apolo@nih.gov. Questions regarding this notice may be directed to Ms. Colleen Watt at cboyle@uchicago.edu. Questions regarding data submission should be directed to Emily Miller at miller.emily4@mayo.edu.

We greatly appreciate your support of this important clinical trial and the work of the Alliance for Clinical Trials in Oncology.

Sincerely,

Andrea Apolo, MD
Alliance A031501 Study Chair