Alliance for Clinical Trials in Oncology
125 S. Wacker Dr., Suite 1600
Chicago IL, 60606
P: 773-702-0956
F: 312-345-0117

www.allianceforclinicaltrialsinoncology.org

June 22, 2021

Dear Alliance A031501 Physician Participant:

This letter is to provide you with information regarding Alliance A031501, "Phase III randomized **A**djuvant study of MK-3475 (pembrolizumab) in mu**S**cle inva**S**ive and locally **Ad**vanced ur**O**thelial ca**R**cinoma" (**AMBASSADOR**) versus observation". As reported in the June 3, 2021 issue of the New England Journal of Medicine, the Checkmate 274 trial (Adjuvant Nivolumab versus Placebo in Muscle-Invasive Urothelial Cancer) met the primary endpoint of disease-free survival. In this trial, in the intention-to-treat population and among patients with a PD-L1 expression level of 1% or more patients with high-risk muscle-invasive urothelial carcinoma who had undergone radical surgery experienced longer disease-free survival with adjuvant nivolumab than those patients who had received placebo. Of note, this population of patients and study design is very similar to that of A031501 with the exception of comparator arm (ie, placebo with CheckMate 274, observation with A031501). It is also important to note that in the March 12, 2021 issue of Lancet Oncology, the study of adjuvant atezolizumab vs observation in muscle-invasive urothelial cancer (IMVIGOR010) reported no improvement in disease-free survival with adjuvant atezolizumab vs observation than those patients who had received placebo. This trial was a negative study for the primary endpoint of disease-free survival.

Although CheckMate 274 yielded positive results, further data from that trial is being processed and, at present, is not an FDA-approved adjuvant indication. Because no change in the current adjuvant treatment landscape for urothelial carcinoma yet has occurred, the National Cancer Institute and the Alliance believe that accrual to A031501 can continue with brief amendments to the informed consent and background section of the protocol to reflect these new developments. Patients already enrolled onto A031501 should receive a "Dear Patient" letter reflecting these updates. A draft of this patient letter accompanies this memorandum. The following actions are now required:

1. Upon receipt of this notice, physicians should discuss the nivolumab and atezolizumab study results with all patients enrolled in this trial. 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. 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 this matter 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.

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