Alliance for Clinical Trials in Oncology
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October 30, 2020

Dear Alliance A051701 Physician Participant:

This letter is to provide you with information regarding Alliance A051701, "Randomized phase II/III study of venetoclax (ABT-199) plus chemoimmunotherapy for MYC/BCL2 double-hit and double expressing lymphomas."

As announced in the broadcast sent on September 1, 2020, the study team noted a possible safety signal among patients with double-hit lymphoma (DHL) who received DA-EPOCH-R-venetoclax, including febrile neutropenia and sepsis. As a result, accrual of patients aged 75 years and older with DHL was temporarily halted on September 1, 2020. Subsequently, as announced by the broadcast sent on September 28, 2020, accrual of all patients with DHL, regardless of age, was temporarily suspended due to a partial clinical hold placed on A051701 by the FDA.

Out of an abundance of caution, the study team elected to discontinue venetoclax dosing in already enrolled patients assigned to the DA-EPOCH-R-venetoclax arm. Investigators at sites with one or more patients currently assigned to this arm were notified on October 20, 2020 to immediately discontinue venetoclax dosing in active DHL patients receiving DA-EPOCH-R-venetoclax.

The following actions are now required:

1. Upon receipt of this notice, physicians should discuss the possible safety signal with patients with DHL enrolled in this trial. To facilitate this discussion, a sample patient letter is available on the Alliance A051701 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 receiving treatment are as follows:
    a. For DHL patients receiving DA-EPOCH-R + venetoclax, discontinue venetoclax dosing immediately. DA-EPOCH-R may continue per protocol.
    b. For patients with DHL receiving DA-EPOCH-R alone, no change to treatment is required.
    c. For patients with DEL receiving R-CHOP with or without venetoclax, no change to treatment is required. This arm remains open to accrual.
3. Required testing, follow-up, and data submission will continue for all randomized patients according to the protocol.

4. 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.

Our top priority remains the safety of all patients enrolled on this study. We continue to analyze the safety data during the partial clinical hold and will be back in touch regarding future plans for re-opening the study to DHL patients with a modified arm for these patients.

Questions regarding the management of individual patients on protocol therapy can be directed to Dr. Jeremy Abramson at jabramson@mgh.harvard.edu. Questions regarding this notice may be directed to Ms. Destin Carlisle at dcarlisle@bsd.uchicago.edu. Questions regarding data submission should be directed to Ms. Ann Hudson at hudson.ann1@mayo.edu.

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

Sincerely,

Jeremy Abramson, MD
Alliance A051701 Study Chair