Alliance for Clinical Trials in Oncology

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June 25, 2020

Dear Alliance A221504 Investigator:

This letter is to provide you with new information regarding A221504, "A Randomized, Double-Blind, Placebo-Controlled Pilot Study of an Oral, Selective Peripheral Opioid Receptor Antagonist In Advanced Non-Small Cell Lung Cancer."

Despite efforts to improve accrual, enrollment has remained insufficient. Alliance has therefore decided to close A221504 to new patient accrual on June 30, 2020. Patients registered on or before this date may continue to receive naloxegol or placebo to allow for as many as 6 months of treatment necessary to achieve study secondary endpoints and follow up.

The following actions are now required:

1) Upon receipt of this letter, physicians should discuss this decision with the patients who are currently receiving treatment on the study. To facilitate this discussion, a sample patient letter is available on the A221504 study page on the members' side of the Alliance and CTSU websites. 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. However, at this time, Investigators should notify their IRB of record and provide copies of this letter and the patient letter.

The Alliance is interested, if patients agree, to continue protocol treatment, required testing, follow-up, and data submission, for up to 6 months from the start of treatment for each patient. As noted above, the study drug will continue to be provided for patients for as many as 6 months from the start of treatment for those patients who choose to remain on protocol treatment. This is to ensure that all patients enrolled on the trial receive sufficient study treatment to meet the Health Related Quality of Life objective at 6 months.

- Subjects just starting treatment will receive a 6 month supply of study drug.
- Subjects who have been on treatment for < 6months will receive sufficient study drug to complete a total of 6 months.
- Subjects who have already been on treatment for 6 months or longer will not receive additional study drug, unless they agree to be unblinded.
- Unblinding is not permitted prior to 6 months of study treatment.
- Subjects and their treating physicians will have the option of being unblinded after 6 months of study treatment. Subjects who agree to be unblinded after completing the 6-month study activities (e.g. completing the HRQoL etc.) but before the 12-month time point, will be allowed to receive naloxegol up to the 12 month time point if they were on active treatment. Subjects who were receiving placebo will not be provided further treatment after unblinding.

cc: P.Gupta, MD

- Subjects who have already received > 12 months of study treatment will not be provided additional study drug (naloxegol or placebo). However, subjects who have already received > 12 months of treatment may choose to be unblinded at any time.
- Please ensure that all study activities (e.g. completing the HRQoL etc.) are completed prior to unblinding each subject.

Questions regarding this notice may be directed to Niveditha Subbiah, A221504 Protocol Coordinator, at nsubbiah@bsd.uchicago.edu or (773) 702 9934.

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

Sincerely,

Selina Chow, MD
Executive Officer
Alliance for Clinical Trials in Oncology