To: Investigators participating in RTOG-0848: A Phase II-R and A Phase III Trial Evaluating Both Erlotinib and Chemoradiation (Ph III) As Adjuvant Treatment For Patients With Resected Head Of Pancreas Adenocarcinoma

From: Ross A. Abrams, MD, Study Chair

Date: May 29, 2014

RE: Erlotinib—Important information regarding lack of efficacy of erlotinib in combination with gemcitabine in locally advanced pancreatic cancer.

The purpose of this letter is to alert investigators of a significant new finding related to erlotinib.

Results of the LAP 07 trial (Hammel, 2013) reported no improvement in overall survival with the addition of erlotinib to gemcitabine in locally advanced pancreatic cancer. In addition, an increased incidence of grade 3 diarrhea was observed in the erlotinib arm, which is consistent with the prescribing information for erlotinib. Given the lack of efficacy evidenced in the LAP 07 trial, NRG Oncology decided to change the evaluation of the effect of erlotinib in RTOG 0848, an adjuvant pancreatic cancer population, to a randomized phase II design and not continue erlotinib in the phase III design. The phase II-R erlotinib randomization (Arm 2) was permanently closed to accrual on April 2, 2014.

Patients currently receiving erlotinib may continue to receive erlotinib on study. Alternatively, patients currently receiving erlotinib may discontinue erlotinib and continue gemcitabine alone on study, or patients may withdraw consent from the study. The plan of care should be carefully considered in light of the new information and in concert with the patient.

Risk Mitigation Plan

Actions Implemented by NRG Oncology:

- Disseminate a Dear Investigator Letter
- Disseminate a Dear Patient Letter
- Amend RTOG-0848 protocol and informed consent document to reflect the change in study design and closure of the erlotinib arm. This was done and broadcasted on April 2, 2014.
- NRG Oncology has expired all IRB approvals with the dissemination of the updated consent and protocol (version date 02/19/14, broadcast on April 2, 2014).

Actions for the Investigator:

- Investigators should promptly inform patients who are currently receiving or have received erlotinib of this significant new finding. The communication of the information should be documented in the medical record.
- For patients enrolled in RTOG-0848 who are in follow-up, i.e. greater than 30 days from end of treatment and no longer receiving erlotinib, this significant new finding should be
communicated during the next scheduled follow-up interval. The communication of the information should be documented in the medical record.

- The amended consent reflects the significant new finding related to erlotinib. Please submit the consent with the new information to your IRB per your local institutional policy. Upon IRB approval, all patients receiving erlotinib must be provided with and sign the amended consent form.

- Review the Dear Patient Letter with all patients who received or are currently receiving erlotinib. For patients currently receiving erlotinib, the decision to continue treatment or pursue one of the alternatives outlined above should be carefully considered. A signed copy of the Dear Patient letter should be saved in the medical record.

Please file a copy of this letter in your protocol file.

If you have any questions regarding this letter, please contact:
  - Ross A. Abrams, MD, Study Chair at 312-942-5751 or by email, ross_a_abrams@rush.edu

Sincerely,

[Signature]

Ross A. Abrams, MD