NRG ONCOLOGY

Advancing Research. Improving Lives.™

memorandum

Four Penn Center • 1600 JFK Blvd, Suite 1020 • Philadelphia, PA 19103
Phone: 215-854-0770 • Fax: 215-854-0716

To: Investigators participating in NRG Oncology study NRG-HN004: Randomized Phase II/III Trial of Radiotherapy with Concurrent MEDI4736 (Durvalumab) vs. Radiotherapy with Concurrent Cetuximab in Patients with Locoregionally Advanced Head and Neck Cancer with a Contraindication to Cisplatin

From: Loren K. Mell, MD

Date: August 9, 2021

RE: Temporary Closure

The purpose of this letter is to inform you of the decision to temporarily close NRG-HN004 to accrual on July 30, 2021.

After review by the NRG Oncology Data Monitoring Committee (DMC) of the study results of a planned interim analysis, the DMC recommended that the phase II portion be closed to accrual. Data from the one planned phase II interim analysis showed that the study crossed the protocol-specified futility threshold for the primary endpoint of progression-free survival (PFS), with an essentially equivocal result between treatment arms with immature data (the median follow-up for PFS is 7 months and 76% of patients are censored). This analysis suggests that the durvalumab arm (Group 2; “study group”) may not meet the protocol hypothesized signal of benefit for PFS compared to cetuximab (Group 1; “usual approach group”) in the final phase II analysis. However, given the close to equivocal early results, the possibility still exists that the trial will show a signal for benefit for the durvalumab arm. For that reason, with the patients already randomized, the phase II portion of the trial will be analyzed with more mature data in approximately 12 months after which a decision regarding re-opening or permanent closure will be made. This decision will be communicated to sites through a broadcast.

The study team has been closely monitoring the grade 5 adverse events due to a higher early death rate up to 200 days after end of concurrent treatment on the durvalumab arm compared to the cetuximab arm [11.5% (14/122) versus 4.8% (3/63)], which does not reach statistical significance at a one-sided alpha of 0.05. This will continue to be monitored carefully. No other unexpected side effects have been seen.

Patients enrolled on NRG-HN004 who are receiving durvalumab and are tolerating treatment may continue to receive drug on study if the patient and the treating physician believe this is an appropriate medical intervention or may receive alternative off-protocol therapy. All study procedures and data collection will continue. Patients enrolled to the cetuximab arm will continue protocol-specified treatment. All protocol-specified procedures and data collection will continue for all randomized patients.

Actions implemented by NRG Oncology:

- Disseminate a Dear Investigator Letter and Dear Patient Letter
- Temporarily close NRG-HN004 to accrual on July 30, 2021

Actions for the Investigator:

- Investigators must submit the Dear Patient Letter to their IRB per local, institutional policy. For sites using the NCI CIRB, this letter has been reviewed and approved.
- Investigators should promptly inform all patients enrolled on NRG-HN004 that the study is temporarily closed to accrual. The communication of the information should be documented in the medical record.
- Patients should receive and review a copy of the Dear Patient Letter. The communication to the patient of this information and their decision regarding continued treatment on study as an appropriate medical intervention or decision to go off of protocol therapy should be documented 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:

- Loren K. Mell, MD, Principal Investigator at 858-246-0471 or lmell@ucsd.edu