ECOG-ACRIN
cancer research group
Reshaping the future of patient care

Operations Office – Boston

April 1, 2021

Dear EA2142 Physician Participant:

We are writing to provide you with an important update regarding EA2142: Randomized Phase II Study of Platinum and Etoposide versus Temozolomide and Capecitabine in Patients with Advanced G3 Non-Small Cell Gastroenteropancreatic Neuroendocrine Tumors including Poorly Differentiated Neuroendocrine Carcinomas and Well-Differentiated Neuroendocrine Neoplasms.

EA2142 was designed and is being conducted by ECOG-ACRIN under its funded cooperative agreement grant with the NCI as part of the NCI National Clinical Trials Network. The primary objective of this trial is to evaluate if the use of temozolomide and capecitabine chemotherapy results in a superior progression free survival as compared to cisplatin/carboplatin and etoposide chemotherapy as front line treatment for patients with high grade neuroendocrine neoplasms.

EA2142 was developed as there has otherwise never been a prospective clinical trial conducted in this patient population, leaving the data lacking in regard to what should be a standard of care. Treatment recommendations thus far have been based on extrapolation from the small cell lung cancer literature. Given the heterogeneity of the high grade (G3) neuroendocrine population and the use of temozolomide and capecitabine in patients with grade 2 neuroendocrine tumors, this was felt to be a possible alternative treatment for this disease, prompting the desire to compare outcomes between temozolomide and capecitabine and platinum/etoposide chemotherapy.

EA2142 was recently reviewed by the ECOG-ACRIN Data Safety and Monitoring Committee as enough PFS events had occurred (65 patients had been accrued). The statistical plan for this trial included an interim analysis to evaluate for futility. This interim analysis was recently completed and it was determined that the boundary for futility has been met. This indicates that temozolomide and capecitabine does not appear to be superior to platinum and etoposide chemotherapy as front line treatment for high grade neuroendocrine neoplasms. Given this finding, it has been recommended that the study be closed due to futility.

We ask that physicians speak with their patients who remain on study specified treatment to determine the best treatment plan moving forward. Temozolomide and capecitabine treatment may be continued per physician discretion if it is believed that the patient is benefiting from treatment and this is considered by the physician and the patient to be an appropriate medical intervention. If it is believed that the patient is not deriving benefit, it may be necessary to offer the patient another treatment option at this time. **These results should be discussed immediately with these patients.**

For those participants who have completed their treatment please share this information at the time of their next study visit.

To facilitate this discussion, and to provide documentation of the participant's willingness to continue participation in the study, we have also prepared a patient directed letter that

28 State Street, Suite 1100, Boston, MA 02109 p: 857.504.2900 f: 617. 589.0914 ecog-acrin.org

summarizes the outcome, has check boxes regarding continued participation, and a signature line.

All discussions should be documented in the patient's medical record.

ECOG-ACRIN and the NCI sincerely appreciate your effort in accruing to this important trial and are grateful for your participation in clinical research.

Questions regarding this notice should be directed to Bruce Giantonio, ECOG-ACRIN Executive Officer, at bgiantonio@ecog-acrin.org.