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Alliance A021901: Randomized Phase II Trial of Lutetium Lu 177 Dotatate Versus Everolimus in Somatostatin Receptor-Positive Bronchial Neuroendocrine Tumors

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BACKGROUND

There is an unmet need for treatment of patients with bronchial neuroendocrine tumors (NETs). Everolimus is FDA approved for the treatment of bronchial NETs based on the RADIANT-4 trial. 177Lu-dotatate is approved for the treatment of gastroenteropancreatic NETs based on the NETTER-1 and NETTER-2 trials. However, there has been no previous clinical trial examining 177Lu-dotatate for bronchial NETs.

METHODS

A021901 (NCT04665739) is an Alliance for Clinical Trials in Oncology / ECOG-ACRIN NCTN cooperative group trial that randomizes patients with metastatic bronchial NETs to receive either everolimus (10 mg oral per day until disease progression or unacceptable toxicity) or 177Lu-dotatate (200 mCi intravenous every eight weeks for four cycles). Randomization is 1:1 between the treatment arms within the stratification factor of prior/concurrent somatostatin analog use. Patients must have well- or moderately-differentiated NETs of bronchial origin (i.e. carcinoid) as assessed by local pathology (including one of the following: well- or moderately-differentiated NET, low- or intermediate-grade NET, or carcinoid tumor including typical or atypical carcinoid tumors). Recurrent or locally advanced/unresectable or metastatic disease that is RECIST 1.1 measurable is required. Patients who are treatment naïve (if disease progression in the last 12 months) and those previously treated (if disease progression on prior line of therapy) are eligible. Baseline somatostatin receptor PET images are centrally reviewed prior to randomization to determine that patients have uptake in all measurable lesions above background liver. Patients are followed every 12 weeks until disease progression, and then every 6 months for survival until 5 years following registration. Patients randomized to everolimus have the option to cross over to receive 177Lu-dotatate at time of progression. The study is designed to accrue a minimum of 70 patients.

RESULTS

The primary objective of A021901 is to compare the radiographic progression-free survival of 177Lu-dotatate to that of everolimus. Secondary objectives include comparing overall survival, overall

response rate, and toxicity profiles between the 177Lu-dotatate and everolimus arms. Exploratory endpoints include evaluation of late toxicities (renal dysfunction and marrow toxicity), impact of baseline tumor volume on treatment response and response rate stratified between typical and atypical bronchial NETs. SPECT/CT images after cycle 1 are acquired as part of exploratory analysis.

CONCLUSIONS

A021901 is currently enrolling in 26 sites in the NCTN cooperative group network with ongoing opportunity for additional sites to activate and accrue. Support: U10CA180821, U10CA180882 (Alliance), U10CA180820 (ECOG-ACRIN), https://acknowledgments.alliancefound.org.

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