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Phase 1-2 Trial of Vesicular Stomatitis Virus Expressing Human Interferon- β and NIS (VSV-IFN β -NIS), with Ipilimumab and Nivolumab, in Patients with Neuroendocrine Carcinoma

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BACKGROUND

Poorly differentiated neuroendocrine carcinoma (NEC) is an aggressive malignancy comprising both pulmonary and extrapulmonary primary sites. NEC includes both small cell lung cancer (SCLC) and large cell neuroendocrine carcinoma (LCNEC). The optimal systemic therapy beyond first line platinum and etoposide is not established. There is a critical need to improve upon the median survival in the second line, as most patients do not survive more than 6 months. The efficacy of single agent immune checkpoint inhibitors (ICIs) in NEC has been disappointing. Dual checkpoint inhibition seems more promising, but response rates are quite modest. One possible explanation for this is that the tumor microenvironment in NEC is non-inflamed. VSV-IFN β -NIS is a vesicular stomatitis virus (VSV)-based oncolytic virus being tested in multiple early phase clinical trials. Preliminary studies of immune responses in patients receiving VSV-IFN β -NIS therapy suggest some patients develop T cell responses to viral antigens and known tumor antigens. We hypothesize that VSV-IFN β -NIS therapy may convert a non-inflamed or immune-excluded phenotype in NEC to a highly inflamed phenotype that sensitizes the tumor to ICIs.

METHODS

This is a phase 1-2 safety run-in study designed to determine the safety of VSV-IFN β -NIS in combination with ipilimumab and nivolumab, followed by dose expansion in patients with refractory non-small cell lung cancer (NSCLC) or NEC. Patients must have previously progressed on at least one line of systemic therapy. Prior treatment with checkpoint inhibitors is permitted. Patients are treated with ipilimumab and nivolumab on day 1, followed by one-time intravenous VSV-IFN β -NIS on day 4, then nivolumab every 3 weeks and ipilimumab every 6 weeks until progression, up to 2 years. The primary objective is to estimate the response rate by RECIST 1.1. Secondary objectives include estimation of disease-control rate, duration of response, progression-free survival, overall survival, and safety signals.

RESULTS

The NEC expansion cohort will seek to enroll 10 patients. If at least one objective response is observed, and safety is confirmed, the regimen will be considered for future study.

CONCLUSIONS

Trial is currently enrolling patients. NCT03647163