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Phase 1-2 Trial of Vesicular Stomatitis Virus Expressing Human Interferon- β and NIS (VSV-IFN β -NIS), with Pembrolizumab, 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), as well as other neuroendocrine carcinomas arising from any primary organ. 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. 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 the PD-1 inhibitor pembrolizumab.

METHODS

This is a phase 1-2 safety run-in study designed to determine the safety of VSV-IFN β -NIS in combination with pembrolizumab, followed by dose expansion in patients with refractory non-small cell lung cancer (NSCLC) or NEC. The safety run-in portion of this study has been completed, and we are presently testing the recommended phase 2 dose (RP2D) of VSV-IFN β -NIS in an expansion cohort of patients with SCLC or NEC of any primary site. Patients must have previously progressed on at least one line of systemic therapy. Prior treatment with checkpoint inhibitors is permitted. Patients are treated with the RP2D of 1.0×10^{11} TCID₅₀ VSV-IFN β -NIS on day 1, followed by pembrolizumab on day 8 and then pembrolizumab every 21 days 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 or 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

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