Patel, S.P., Othus, M., Chae, et al 2020. **A Phase II Basket Trial of Dual Anti-CTLA-4 and Anti-PD-1 Blockade in Rare Tumors (DART SWOG 1609) in Patients with Non-Pancreatic Neuroendocrine Tumors.** Clin Cancer Res 26, 2290–2296. https://doi.org/10.1158/1078-0432.CCR-19-3356

Abstract

Purpose: Immune checkpoint blockade has improved outcomes across tumor types; little is known about the efficacy of these agents in rare tumors. We report the results of the (nonpancreatic) neuroendocrine neoplasm cohort of SWOG S1609 dual anti-CTLA-4 and anti-PD-1 blockade in rare tumors (DART).

Patients and methods: We performed a prospective, open-label, multicenter phase II clinical trial of ipilimumab plus nivolumab across multiple rare tumor cohorts, with the (nonpancreatic) neuroendocrine cohort reported here. Response assessment by grade was not prespecified. The primary endpoint was overall response rate [ORR; RECIST v1.1; complete response (CR) and partial response (PR)]; secondary endpoints included progression-free survival (PFS), overall survival (OS), stable disease >6 months, and toxicity.

Results: Thirty-two eligible patients received therapy; 18 (56%) had high-grade disease. Most common primary sites were gastrointestinal (47%; $N = 15$) and lung (19%; $N = 6$). The overall ORR was 25% [95% confidence interval (CI) 13-64%; CR, 3%, $N = 1$; PR, 22%, $N = 7$]. Patients with high-grade neuroendocrine carcinoma had an ORR of 44% (8/18 patients) versus 0% in low/intermediate grade tumors (0/14 patients; $P = 0.004$). The 6-month PFS was 31% (95% CI, 19%-52%); median OS was 11 months (95% CI, 6-∞). The most common toxicities were hypothyroidism (31%), fatigue (28%), and nausea (28%), with alanine aminotransferase elevation (9%) as the most common grade 3/4 immune-related adverse event, and no grade 5 events.

Conclusions: Ipilimumab plus nivolumab demonstrated a 44% ORR in patients with nonpancreatic high-grade neuroendocrine carcinoma, with 0% ORR in low/intermediate grade disease.
Trial registration: ClinicalTrials.gov NCT02834013.