Nivolumab plus platinum-doublet chemotherapy in treatment-naive patients with advanced grade 3 Neuroendocrine Neoplasms of gastroenteropancreatic or unknown origin: The multicenter phase 2 NICE-NEC trial (GETNE-T1913)

The prognosis of patients with advanced high-grade (G3) digestive neuroendocrine neoplasms (NENs) is rather poor. The addition of immune checkpoint inhibition to platinum-based chemotherapy may improve survival. NICE-NEC (NCT03980925) is a single-arm, phase II trial that recruited chemotherapy-naive, unresectable advanced or metastatic G3 NENs of gastroenteropancreatic (GEP) or unknown origin. Patients received nivolumab 360 mg intravenously (iv) on day 1, carboplatin AUC 5 iv on day 1, and etoposide 100 mg/m2/d iv on days 1-3, every 3 weeks for up to six cycles, followed by nivolumab 480 mg every 4 weeks for up to 24 months, disease progression, death or unacceptable toxicity. The primary endpoint was the 12-month overall survival (OS) rate (H_0 50%, H_1 72%, β 80%, α 5%). Secondary endpoints were objective response rate (ORR), duration of response (DoR), progression-free survival (PFS), and safety. From 2019 to 2021, 37 patients were enrolled. The most common primary sites were the pancreas (37.8%), stomach (16.2%) and colon (10.8%). Twenty-five patients (67.6%) were poorly differentiated carcinomas (NECs) and/or had a Ki67 index >55%. The ORR was 56.8%. Median PFS was 5.7 months (95%CI: 5.1-9) and median OS 13.9 months (95%CI: 8.3-Not reached), with a 12-month OS rate of 54.1% (95%CI: 40.2-72.8) that did not meet the primary endpoint. However, 37.6% of patients were long-term survivors (>2 years). The safety profile was consistent with previous reports. There was one treatment-related death. Nivolumab plus platinum-based chemotherapy was associated with prolonged survival in over one-third of chemonaïve patients with G3 GEP-NENs, with a manageable safety profile.

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