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Amrubicin in patients with platinum-refractory metastatic neuroendocrine carcinoma of the gastrointestinal tract

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Introduction: Patients with gastrointestinal neuroendocrine carcinoma (GI-NEC) have a poor prognosis. Platinum-based combination chemotherapy is commonly used as first-line treatment; however, there are a few reports about the role of amrubicin (AMR) and salvage chemotherapy for GI-NEC. This study aimed to analyze the efficacy and safety of AMR monotherapy in patients with platinum-refractory GI-NEC.

Methods: We retrospectively analyzed platinum-refractory GI-NEC patients who received AMR monotherapy between April 2012 and September 2017 at the Cancer Institute Hospital. The dose of AMR administered was 30–45 mg/m2 on days 1–3 every 3–4 weeks. We evaluated the overall response rate (ORR) according to the RESICT ver.1, progression-free survival (PFS), overall survival (OS), and adverse events by CTCAE ver.4.0. OS and PFS were estimated using the Kaplan-Meier method and compared using the log-rank test. All reported P values were the result of two-sided tests; P < 0.05 was considered significant.

Results: 14 males and 3 females (median age, 65 years [range, 60–75]) were received platinum-based chemotherapy before AMR monotherapy: cisplatin plus irinotecan (n = 14, 82.3%), cisplatin plus etoposide (n = 1, 5.9%), and fluoropyrimidine plus platinum (n = 2, 11.8%) Primary sites of NEC included stomach (n = 10, 58.8%), colorectal (n = 3, 17.6%), esophagus (n = 3, 17.6%), and duodenum (n = 1, 5.9%). The median cycles of AMR administration were 3 (range, 1–15). The ORR rate was 5.8%, the median PFS was 2.1 months (1.4–6.9), and the median OS was 13.7 months (6.9–17.2). Grade 3/4 neutropenia occurred in 41.1% of patients and febrile neutropenia occurred in 5.8%. Other non-hematological toxicities were not severe and treatment related deaths were not observed. 11 patients received the subsequent chemotherapy after AMR and they had significantly longer OS than those who couldn’t be received the subsequent chemotherapy. (17.2 months (5.9–NA) vs. 8.9 months (1.1–NA), p = 0.0427).

Conclusion: AMR showed minimum activity and safety when used for the treatment of platinum-refractory GI-NEC. Neutropenia was encountered as the most serious adverse event. It should be considered to perform the subsequent chemotherapy after AMR if possible.