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Gemcitabine, carboplatin and veliparib in multiple relapsed/refractory germ cell tumours: The GCT-SK-004 phase II trial

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Abstract

Background Patients with multiple relapsed/refractory germ cell tumours (GCTs) have an extremely poor prognosis. PARP (poly-ADP-ribose polymerase) is overexpressed in GCTs compared to normal testes, and PARP overexpression is an early event in GCT development. This study aimed to determine the efficacy and toxicity of gemcitabine, carboplatin and the PARP inhibitor veliparib in patients with multiple relapsed/refractory GCTs. Methods Fifteen patients with multiple relapsed/refractory GCTs were enrolled in this phase II study from October 2016 to October 2020. Gemcitabine was administered at a dose of 800 mg/m2 on days 1 and 8 every 3 weeks; carboplatin at a target AUC of 4 on day 1 every 3 weeks; and veliparib at a dose of 250 mg b.i.d. throughout. The primary end point was 12-month progression-free survival (PFS). Results The median number of treatment cycles was 4 (range 2-8). Twelve-month PFS was achieved in 1 (6.7 %) patient. The median PFS was 3.1 months (95 % CI 2.2-3.9), and the median overall survival was 10.5 months (95 % CI 8.9-11.1). Partial remission was achieved in 4 (26.7 %) patients, and disease stabilization was observed in 5 (33.3 %) patients. A favourable response was achieved in 3 (20.0 %) patients. Treatment was well tolerated; however, 11 (73.3 %) patients experienced grade 3/4 neutropenia, 10 (66.7 %) experienced thrombocytopenia, 5 (33.3 %) anaemia and 2 (13.3 %) febrile neutropenia. Conclusions This study failed to achieve its primary endpoint, and our data suggest limited efficacy of gemcitabine, carboplatin and veliparib for multiple relapsed/refractory GCTs. ClinicalTrials.gov Identifier: NCT02860819, registered August 9, 2016.

Keywords: Carboplatin; Gemcitabine; Germ cell tumours; PARP; Refractory; Veliparib.