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GENITOURINÁRNE MALIGNITY

Mego M, Svetlovska D, Reckova M, Angelis D, Kalavska K, Obertova J, Palacka P, Rejlekova K, Sycova-Mila Z, Chovanec M, Mardiak J.

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

Invest New Drugs. 2021 May 29. doi: 10.1007/s10637-021-01130-5.

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/m^2 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.

Schmidtova S, Kalavska K, Liskova V, Plava J, Miklikova S, Kucerova L, Matuskova M, Rojikova L, Cierna Z, Rogozea A, Konig H, Albany C, **Mego M, Chovanec M.**

Targeting of Deregulated Wnt/β-Catenin Signaling by PRI-724 and LGK974 Inhibitors in Germ Cell Tumor Cell Lines

Int J Mol Sci. 2021 Apr 20;22(8):4263.

The majority of patients with testicular germ cell tumors (GCTs) can be cured with cisplatin-based chemotherapy. However, for a subset of patients present with cisplatin-refractory disease, which confers a poor prognosis, the treatment options are limited. Novel therapies are therefore urgently needed to improve outcomes in this challenging patient population. It has previously been shown that Wnt/β-catenin signaling is active in GCTs suggesting that its inhibitors LGK974 and PRI-724 may show promise in the management of cisplatin-refractory GCTs. We herein investigated whether LGK-974 and PRI-724 provide a treatment effect in cisplatin-resistant GCT cell lines. Taking a genoproteomic approach and utilizing xenograft models we found the increased level of β-catenin in 2 of 4 cisplatin-resistant (CisR) cell lines (TCam-2 CisR and NCCIT CisR) and the decreased level of β-catenin and cyclin D1 in cisplatin-resistant NTERA-2 CisR cell line. While the effect of treatment with LGK974 was limited or none, the NTERA-2 CisR exhibited the increased sensitivity to PRI-724 in comparison with parental cell line. Furthermore, the pro-apoptotic effect of PRI-724 was documented in all cell lines. Our data strongly suggests that a Wnt/β-catenin signaling is altered in cisplatin-resistant GCT cell lines and the inhibition with PRI-724 is effective in NTERA-2 CisR cells. Further evaluation of Wnt/β-catenin pathway inhibition in GCTs is therefore warranted.

NÁDORY HLAVY A KRKU

Svajdova M, Sicak M, Dubinsky P, Slavik M, Slampa P, Kazda T.

Recurrent Nasopharyngeal Cancer: Critical Review of Local Treatment Options Including Recommendations during the COVID-19 Pandemic

Cancers (Basel). 2020 Nov 25;12(12):3510.

Recurrent nasopharyngeal carcinoma represents an extremely challenging therapeutic situation. Given the vulnerability of the already pretreated neurological structures surrounding the nasopharynx, any potential salvage retreatment option bears a significant risk of severe complications that result in high treatment-related morbidity, quality of life deterioration, and even mortality. Yet, with careful patient selection, long-term survival may be achieved after local retreatment in a subgroup of patients with local or regional relapse of nasopharyngeal cancer. Early detection of the recurrence represents the key to therapeutic success, and in the case of early stage disease, several curative treatment options can be offered to the patient, albeit with minimal support in prospective clinical data. In this article, an up-to-date review of published evidence on modern surgical and radiation therapy treatment options is summarized, including currently recommended treatment modifications of both therapeutic approaches during the coronavirus disease 2019 pandemic.

Svajdova M, Dubinsky P, Kazda T.

Radical external beam re-irradiation in the treatment of recurrent head and neck cancer: Critical review

Head Neck. 2021 Jan;43(1):354-366.

Management of patients with recurrent head and neck cancer remains

a challenge for the surgeon as well as the treating radiation oncologist. Even in the era of modern radiotherapy, the rate of severe toxicity remains high with unsatisfactory treatment results. Intensity-modulated radiation therapy (IMRT), stereotactic body radiation therapy (SBRT), and heavy-ion irradiation have all emerged as highly conformal and precise techniques that offer many radiobiological advantages in various clinical situations. Although re-irradiation is now widespread in clinical practice, little is known about the differences in treatment response and toxicity using diverse re-irradiation techniques. In this review, we provide a comprehensive overview of the role of radiation therapy in recurrent or second primary head and neck cancer including patient selection, therapeutic outcome, and risk using different re-irradiation techniques. Critical review of published evidence on IMRT, SBRT, and heavy-ion full-dose re-irradiation is presented including data on locoregional control, overall survival, and toxicity.

Abstrakty a príspevky z konferencií

GENITOURINÁRNE MALIGNITY

Palacka P, Slopovsky J, Zanchetta K, Drgona L, Badurikova E, Bernadicova B, Baranova V, Pechan J, Mego M.
Incidence of tozinameran adverse events among the employees of National Cancer Institute.
J Clin Oncol 39, 2021 (suppl 15; abstr e18724)

Rejlekova K, Kalavska K, Makovnik M, Hapakova N, Chovanec M, De Angelis V, Obertova J, Palacka P, Sycova-Mila Z, Mardiak J, Mego M.
Predictive factors for choriocarcinoma syndrome development in high-risk patients with germ cell tumors (GCTs).
J Clin Oncol 39, 2021 (suppl 15; abstr e17010)

Mego M, Svetlovska D, Reckova M, Kalavska K, Obertova J, Palacka P, Rejlekova K, De Angelis V, Sycova-Mila Z, Chovanec M, Mardiak J.
Phase II study of gemcitabine, carboplatin and veliparib in multiple relapsed/refractory germ cell tumors (GCTs).
J Clin Oncol 39, 2021 (suppl 15; abstr e17009)

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Burden of chemotherapy-induced peripheral neuropathy and associations with long-term sexual impairment in testicular germ cell tumor survivors.
J Clin Oncol 39, 2021 (suppl 15; abstr e17014)