POSTERS

P-1 Potential neuroprotective effects of losartan and donepezil on oxaliplatin-induced peripheral neuropathy in rats

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Background: Oxaliplatin (OXL) is a platinum-based antineoplastic drug widely used for treating colorectal cancer which induces peripheral neuropathy as dose-limiting toxicity. We assess the neuroprotective effects of losartan (LOS) and donepezil (DPZ) on OXL-induced peripheral neuropathy in rats.

Methods: Forty Sprague-Dawley rats were divided into four groups; control (vehicle-treated), OXL (2.4 mg/kg/d; intraperitoneal), OXL+LOS (100 mg/kg/d; oral), and OXL+DPZ (1 mg/kg/d; oral). All were given 5 times/week for 2 weeks. Behavioral assessment of pain, sensory, and motor disturbances was done on days 7 and 14 using a paintbrush, acetone, tail-flick latency, and grip strength tests. The levels of interleukin (IL)-1β, and tumor necrosis factor (TNF)-α were measured in L4-L6 samples. Histopathological examination of the sciatic nerve was done to assess nerve degeneration.

Results: OXL induced significant mechanical dynamic allodynia, cold allodynia, and thermal hyperalgesia compared to the control group. LOS significantly ameliorated mechanical and cold allodynia, while DPZ improved mechanical allodynia and thermal hyperalgesia. OXL significantly increased IL-1β, and TNF-α compared to the control group. Only LOS significantly attenuated these markers. In the OXL group, the axons were swollen, and nerve fiber degeneration with neuron gaps occurred. Both treatments improved these histopathological changes.

Conclusions: LOS and DPZ attenuate the neurotoxic effect of oxaliplatin by attenuating behavioral and histopathological alterations and the protective effect of LOS may involve in the inhibition of spinal pro inflammatory cytokines. Therefore, LOS and DPZ are promising agents to prevent OXA-induced peripheral neuropathy.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.093

P-2 Modified GTX second-line therapy in pancreatic adenocarcinoma: An updated analysis

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Background: To date, no standard of care for second-line therapy of advanced pancreatic adenocarcinoma has been established for patients progressing on first-line FOLFIRINOX or Gemzar/Abraxane. [1] The use of a modified regimen of Gemcitabine, Docetaxel, and Capecitabine (GTX) has been suggested following considerable evidence which showed GTX-induced synergistic apoptosis of human pancreatic cancer cells. [2] Retrospective analysis of GTX regimen use, previously conducted at our institution, has shown good tolerability in this patient population with a response rate of 33%. [3] The aim of this prospective analysis is to evaluate the radiological response rates, toxicity and survival of modified GTX in advanced pancreatic cancer patients progressing on first-line chemotherapy.

Methods: 41 patients presenting to the American University of Beirut Medical Center (AUBMC) between March 2013 and December 2021 with locally advanced unresectable or metastatic pancreatic adenocarcinoma and progressing on first-line chemotherapy were eligible for the study. Patients received modified GTX that consisted of: -Intravenous administration of Docetaxel (40mg/m2) on days 1 and 15. -Intravenous administration of Gemcitabine (1000mg/m2) on days 8 and 22. -Oral administration of Capecitabine (625mg/m2) twice daily on days 6-10 and 20-24. GTX cycles were repeated every 28 days as second-line treatment or beyond.

Results: The mean age at diagnosis was 56.54 years (range: 36-82). Mean follow-up in this cohort was 7.92 months.The mean number of GTX cycles was 3.95 (range: 2-18). According to RECIST guidelines, within the whole cohort, 26 patients had progression (66.7%), 10 had stable response (25.6%) and 3 had partial response (7.7%) after 3 months of treatment. Median overall survival (OS) for all patients was 7 months, ranging from 2 months to 45 months after the date of diagnosis. Median progression free survival (PFS) for all patients was 2 months, ranging from 1 month to 31 months after the date of diagnosis. The percentage of patients treated with GTX as second-line therapy was 41.5% (17/41) and as third-line and beyond was 58.5% (24/41). Median OS for the 17 patients on second-line therapy was 5 months, ranging from 2 to 45 months. The remaining 24 patients on third-line treatment had an OS of 8 months ranging from 2 to 18 months (p=0.449). Median PFS for the 17 patients on second-line was 2 months, ranging from 1 to 31 months. 23 patients on third-line had a PFS of 3 months ranging from 1 to 9 months (p=0.587). From the patients receiving GTX as second-line treatment, 75% had progression compared to 61% from those receiving it as third line, with p=0.495. (Fischer exact test). Patients receiving GTX had some adverse events such as anemia (97.5%), neutropenia (50%), thrombocytopenia (22.5%), mucositis (32.5%), nausea and vomiting (17.5%), diarrhea (20%) and infection (22.5%).

Conclusions: GTX could be used as second-line therapy in advanced pancreatic adenocarcinoma with a tolerable toxicity profile. Further prospective studies with larger samples should be performed for better assessment.

Legal entity responsible for the study: The authors.

Funding: Has not received any funding.

Disclosures: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.094

P-3 Gastric cancer prognosis and cell ratio factors

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Background: We examined cell ratio factors (CRF) significantly affecting gastric cancer (EC) patients GCP) survival. CRF - ratio between cancer cells (CC) and blood cells subpopulations.

Methods: We analyzed data of 799 consecutive GCP (T1-4N0-2M0) (age=57.1±9.4 years; tumor size=5.4±3.1 cm) radically operated (R0) and monitored in 1975-2022 (m=558, f=241; total gastrectomies=173, distal gastrectomies=461; proximal gastrectomies=165; combined gastrectomies=247 with resection of esophagus, pancreas, liver, duodenum, diaphragm, colon transversum, splenectomy, etc; only surgery-S=624, adjuvant chemoimmunotherapy-AT=175 (5-FU + thymalin/taktivin); T1=238, T2=220, T3=184, T4=157; N0=437, N1=109, N2=253, M0=799; G1=222, G2=164, G3=413. Variables selected for prognosis study were input levels of 45 blood parameters, sex, age, TNMG, cell type, tumor size. Survival curves were estimated by the Kaplan-Meier method. Differences in curves between groups of GCP were evaluated using a log-rank test. Multivariate Cox modeling, discriminant analysis, clustering, SEPATH, Monte Carlo, bootstrap and neural networks computing were used to determine any significant dependence.

Results: Overall life span (LS) was 2128.9±2300.3 days and cumulative 5-year survival (5YS) reached 58.4%, 10 years — 51.9%, 20 years — 39%, 30 years — 27.2%. 318 GCP lived more than 5 years (LS=4304.5±2290.6 days), 169 ECP — more than 10 years (LS=5919.5±2020 days). 290 GCP died because of GC (LS=651±347.2 days). Cox modeling displayed that ECP survival significantly depended on CRF: healthy cells/CC, erythrocytes/CC, monocytes/CC, phase transition (PT) in terms of synergetics early-invasive cancer; PT N0–N12, age, G1-3, hemorrhage time, ESS, sex, AT, prothrombin index, residual nitrogen. Neural networks, genetic algorithm selection and bootstrap simulation revealed relationships between 5YS and PT early-invasive cancer (rank=1); PT N0–N12 (2); healthy cells/CC (3), erythrocytes/CC (4), thrombocytes/CC (5), monocytes/CC (6), segmented neutrophils/CC (7), leucocytes/CC (8), lymphocytes/CC (9), stick neutrophils/CC (10), eosinophils/CC (11). Correct prediction of 5YS was 100% by neural networks computing (area under ROC curve=1.0; error=0.0).

Conclusions: GCP survival after radical procedures significantly depended on CRF.

Legal entity responsible for the study: The author.

Funding: Has not received any funding.

Disclosures: The author has declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2022.04.095