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GENITOURINÁRNE MALIGNITY

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Prognostic role of plasma vitamin D and its association with disease characteristics in germ cell tumours

Front Oncol. 2023 Apr 11;13:1149432.

Background: Testicular cancer is the most common malignancy among young men. Vitamin D has pluripotent effects on cancer pathogenesis and plays a role in the metastatic cascade. The aim of this study is to analyze plasma vitamin D in association with clinico-pathological findings and prognosis in patients with germ-cell tumors (GCTs).

Methods: This study included 120 newly diagnosed and/or relapsed GCT patients treated from April 2013 to July 2020, for whom plasma was available in the biobank. Blood samples were drawn the 1st chemotherapy cycle as well as before the 2nd cycle. Plasma vitamin D was measured using ELISA and correlated with disease characteristics and the outcome. For survival analysis, the cohort was dichotomized into "low" and "high" based on median vitamin D.

Results: There was no significant difference in vitamin D plasma levels between healthy donors and GCT patients (p = 0.71). Vitamin D level was not associated with disease characteristics except for brain metastases, where patients with brain metastases had a vitamin D level that was 32% lower compared to patients without brain metastases, p = 0.03. Vitamin D was also associated with response to chemotherapy, with an approximately 32% lower value in patients with an unfavorable response compared to a favorable response, p = 0.02. Moreover, low plasma levels of vitamin D were significantly associated with disease recurrence and inferior progression-free survival (PFS), but not with overall survival (OS) (HR = 3.02, 95% CI 1.36-6.71, p = 0.01 for PFS and HR = 2.06, 95% CI 0.84-5.06, p = 0.14 for OS, respectively).

Conclusion: Our study suggests the prognostic value of pretreatment vitamin D concentrations in GCT patients. Low plasma vitamin D was associated with an unfavorable response to therapy and disease recurrence. However, it remains to be determined whether the biology of the disease confirms a causative role for low vitamin D and whether its supplementation affects the outcome.

Chovanec M, Kalavska K, Obertova J, Palacka P, Rejlekova K, Sycova-Mila Z, Orszaghova Z, Lesko P, De Angelis V, Vasilkova L, Svetlovska D, Mladosievicova B, Mardiak J, Pastorek M, Vlkova B, Celec P**, Mego M.**

Cognitive impairment and biomarkers of gut microbial translocation in testicular germ cell tumor survivors

Front Oncol. 2023 Mar 21;13:1146032.

Background: Survivors of testicular germ cell tumors (GCT) may suffer from late cognitive impairment. We hypothesized that disruption of intestinal barrier during chemotherapy and/or radiotherapy may be a contributing factor of cognitive dysfunction within the gut-blood-brain axis.

Methods: GCT survivors (N = 142) from National Cancer Institute of Slovakia completed the Functional Assessment of Cancer Therapy Cognitive Function questionnaires during their annual follow-up visit at 9-year median (range 4-32). Biomarkers of gut microbial translocation and dysbiosis high mobility group box-1 (HMGB-1), lipopolysaccharide, d-lactate and sCD14 were measured from peripheral blood obtained during the same visit. Each questionnaire score was correlated with biomarkers. Survivors were treated with orchiectomy only (N = 17), cisplatin-based chemotherapy (N = 108), radiotherapy to the retroperitoneum (N = 11) or both (N = 6).

Results: GCT survivors with higher sCD14 (above median) had worse cognitive function perceived by others (CogOth domain) (mean ± SEM; 14.6 ± 0.25 vs 15.4 ± 0.25, p = 0.019), lower perceived cognitive abilities (CogPCA domain) (20.0 ± 0.74 vs 23.4 ± 0.73, p = 0.025) and lower overall cognitive function score (109.2 ± 0.74 vs 116.7 ± 1.90, p = 0.021). There were no significant cognitive declines associated with HMGB-1, d-lactate and lipopolysaccharide. Survivors treated with ≥ 400mg/m2 vs < 400mg/m2 of cisplatin-based chemotherapy had a higher lipopolysaccharide (567.8 µg/L ± 42.7 vs 462.9 µg/L ± 51.9, (p = 0.03).

Conclusions: sCD14 is a marker of monocytic activation by lipopolysaccharide and may also serve as a promising biomarker of cognitive impairment in long-term cancer survivors. While chemotherapy and radiotherapy-induced intestinal injury may be the underlying mechanism, further research using animal models and larger patient cohorts are needed to explore the pathogenesis of cognitive impairment in GCT survivors within the gut-brain axis.

Antonelli L, Ardizzone D, Ravi P, Bagrodia A, **Mego M**, Daneshmand S, Nicolai N, Nazzani S, Giannatempo P, Franza A, Heidenreich A, Paffenholz P, Saoud R, Eggener S, Ho M, Oswald N, Olson K, Tryakin A, Fedyanin M, Naoun N, Javaud C, Fizazi K, King JM, Adra N, Douglawi A, Cary C, Sweeney C, Fankhauser CD.

Risk of residual cancer after complete response following first-line chemotherapy in men with metastatic non-seminomatous germ cell tumour and International Germ Cell Cancer Cooperative Group intermediate/poor prognosis: A multi-institutional retrospective cohort study

Eur J Cancer. 2023 Mar;182:144-154.

Introduction: Current guidelines recommend surveillance in metastatic non-seminomatous germ cell tumour patients treated with first-line-chemo-

therapy and a complete clinical response (normalisation of serum tumour markers and residual masses <1 cm). However, this recommendation is based on a series including patients with good prognosis according to International Germ Cell Cancer Cooperative Group prognostic group (IGCCCG-PG). The aim of this study was to analyse the proportion of residual teratoma and survival among patients with intermediate/poor IGCCCG-PG and a complete clinical response after first-line-chemotherapy.

Material and methods: This is a retrospective study of men with intermediate/poor IGCCCG-PG, who had a complete clinical response after first-line chemotherapy. Patients were either followed by surveillance or treated with post-chemotherapy retroperitoneal lymph node dissection (pcRPLND).

Results: Between 2009 and 2018, 143 men with intermediate (n = 83) or poor (n = 60) IGCCCG-PG were treated at 11 international centres. Among 33 patients treated with pcRPLND, the specimen showed teratoma and viable cancer in 16 (48%) and 4 (12%). During a median a 7-year follow-up, 20/110 (18%) patients managed with surveillance relapsed, of whom seven (6%) had a retroperitoneal-only relapse versus 2/33 patients managed with pcRPLND relapsed. No difference was observed regarding overall survival (OS) among men treated with pcRPLND or surveillance (5-year OS, 93% and 89%, p-value = 0.35). The median time-to-recurrence among men on surveillance was 1.3 years (range: 0.3-9.1), and the most common sites of relapses included retroperitoneum (11%), chest (5%), and bones (4%).

Conclusions: While most men with intermediate/poor IGCCCG-PG harbour teratoma/cancer in the retroperitoneum despite a complete response to first-line--chemotherapy, only 6% managed with surveillance relapsed in the retroperitoneum. There was no significant difference in OS between the two groups.

GASTROINTESTINÁLNE MALIGNITY

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Alcoholic Liver Disease-Related Hepatocellular Carcinoma: Characteristics and Comparison to General Slovak Hepatocellular Cancer Population

Curr Oncol. 2023 Mar 22;30(3):3557-3570.

Hepatocellular carcinoma (HCC) has multiple molecular classes that are associated with distinct etiologies and, besides particular molecular characteristics, that also differ in clinical aspects. We aim to characterize the clinical aspects of alcoholic liver disease-related HCC by a retrospective observational study that included all consequent patients diagnosed with MRI or histologically verified HCC in participating centers from 2010 to 2016. A total of 429 patients were included in the analysis, of which 412 patients (96%) had cirrhosis at the time of diagnosis. The most common etiologies were alcoholic liver disease (ALD) (48.3%), chronic hepatitis C (14.9%), NAFLD (12.6%), and chronic hepatitis B (10%). Patients with ALD-related HCC were more commonly males, more commonly had cirrhosis that was in more advanced stages and had poorer performance status. Despite these results, no differences were observed in the overall (median 8.1 vs. 8.5 months) and progression-free survival (median 4.9 vs. 5.7 months). ALD-HCC patients within BCLC stage 0-A less frequently received potentially curative treatment as compared to the control HCC patients (62.2% vs. 87.5%, p = 0.017); and in patients with ALD-HCC liver function (MELD score) seemed to have a stronger influence on the prognosis compared to the control group HCC. Systemic inflammatory indexes were strongly associated with survival in the whole cohort. In conclusion, alcoholic liver disease is the most common cause of hepatocellular carcinoma in Slovakia, accounting for almost 50% of cases; and patients with ALD-related HCC more commonly had cirrhosis that was in more advanced stages and had poorer performance status, although no difference in survival between ALD-related and other etiology-related HCC was observed.

HEMATOLOGICKÉ MALIGNITY

van Doesum JA, Salmanton-García J, Marchesi F, Di Blasi R, Falces-Romero I, Cabirta A, Farina F, Besson C, Weinbergerová B, Van Praet J, Schönlein M, Lopez-Garcia A, Lamure S, Guidetti A, De Ramón-Sánchez C, Batinic J, Gavriilaki E, Tragiannidis A, Tisi MC, Plantefeve G, Petzer V, Ormazabal-Velez I, Marques de Almeida J, Marchetti M, Maertens JA, Machado M, Kulasekararaj AG, Hernández-Rivas JÁ, Gomes da Silva M, Fernández N, Espigado I, **Drgona L**, Dragonetti G, Metafuni E, Calbacho M, Blennow O, Wolf D, van Anrooij B, Nunes Rodrigues R, Nordlander A, Martín-González JA, Lievin R, Jiménez M, Grafe SK, Garcia-Sanz R, Córdoba R, Rahimli L, van Meerten T, Cornely OA, Pagano L.

Impact of SARS-CoV-2 vaccination and monoclonal antibodies on outcome post CD19-CAR-T: an EPICOVIDEHA survey

Blood Adv. 2023 (In press)

Patients with previous CD19 directed chimeric antigen receptor T cell therapy (CAR T)-cell therapy have a prolonged vulnerability to viral infections. Coronavirus diseases 2019 (COVID-19) has a great impact and has previously been shown to cause high mortality in this population. Until now, real world data of the impact of vaccination and treatment on patients with COVID-19 after CD19 directed CAR T-cell therapy are lacking. Therefore, this multicenter retrospective study was conducted with data from the EPICOVIDEHA survey. Sixty-four patients were identified. The overall mortality caused by COVID-19 was 31%. Patients infected with the Omicron variant had a significantly lower risk of death due to COVID-19 compared to patients infected with previous variants (7% versus 58% (P=0.012)). Twenty-six patients were vaccinated at time of COVID-19 diagnosis. Two vaccinations showed marked but unsignificant reduction risk of COVID-19 caused mortality (33.3% versus 14.2% (P=0.379)). Also the course of disease appears milder with less frequent ICU admissions (39% versus 14% (P=0.054)) and shorter duration of hospitalization (7 versus 27.5 days (P=0.022)). Of the available treatment options, only monoclonal antibodies seemed to be effectively reducing mortality from 32% to zero (P=0.036). We conclude that survival rates of CAR T-cell recipients with COVID-19 improved over time and that the combination of prior vaccination and monoclonal antibody treatment significantly reduces their risk of death.