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PODPORNÁ LIEČBA

Mego M, Danis R, Chovanec J, Jurisova S, Bystricky B, Porsok S, Konkolovsky P, Vaclav V, Wagnerova M, Streško M, Brezinova B, Rečková M, Sutekova D, Pazderova N, Novisedlakova M, Zomborska E, Ciernikova S, Svetlovska D, Drgona L. **Randomized double-blind, placebo-controlled multicenter phase III study of prevention of irinotecan-induced diarrhea by a probiotic mixture containing Bifidobacterium BB-12® Lactobacillus rhamnosus LGG® in colorectal cancer patients**

Front Oncol. 2023 Aug 4;13:1168654.

Background: The incidence of irinotecan-induced diarrhea varies between 60–90%, by which the incidence of severe diarrhea is 20–40%. The objective of this phase III trial was to determine the effectiveness of the probiotic mixture containing Bifidobacterium, BB-12® and Lactobacillus rhamnosus, LGG® in the prophylaxis of irinotecan-induced diarrhea in metastatic colorectal cancer patients due to a reduction in the activity of intestinal beta-D-glucuronidase.

Methods: From March 2016 to May 2022, a total of 242 patients with colorectal cancer starting a new line of irinotecan-based therapy were registered to the study in 11 cancer centers in Slovakia. Patients were randomized in a ratio 1:1 to probiotic formula vs. placebo that was administered for 6 weeks. Each capsule of Probio-Tec® BG-Vcap-6.5 contained 2.7x10⁹ colony-forming units (CFU) of 2 lyophilized probiotic strains Bifidobacterium, BB-12® (50%) and Lactobacillus rhamnosus GG, LGG® (50%).

Results: Administration of probiotics compared to placebo was not associated with a significant reduction of grade 3/4 diarrhea (placebo arm 11.8% vs. probiotic arm 7.9%, p=0.38). Neither the overall incidence of diarrhea (46.2% vs. 41.2%, p=0.51) nor the incidence of enterocolitis (3.4% vs. 0.9%, p=0.37) was different in the placebo vs. probiotic arm.

Subgroup analysis revealed that patients with colostomy had higher incidence of any diarrhea and grade 3/4 diarrhea in the placebo arm compared to the probiotic arm (48.5% vs. 22.2%, p=0.06 and 15.2% vs. 0%, p=0.06, respectively). Moreover, patients on probiotic arm had significantly better diarrhea-free survival (HR = 0.41, 95%CI 0.18 - 0.95, p=0.05) and needed less loperamide (p=0.01) compared to patients on placebo arm. We did not observe any infection caused by probiotic strains used in this study.

Conclusion: This study failed to achieve its primary endpoint, and results suggest a lack of benefit of administered probiotic formula for the prevention of irinotecan-induced diarrhea. However, subgroup analysis suggests a possible benefit in patients with colostomy.

GENITOURINÁRNE MALIGNITY

Antonelli L, Ardizzone D, Tachibana I, Adra N, Cary C, Hugar L, Sexton WJ, 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, Cazzaniga W, Nicol D, Gerdtsson A, Tandstad T, Fizazi K, Fankhauser CD; EAU-YAU Penile and Testis Cancer Working Group.

Risk Factors for Relapse in Nonseminomatous Testicular Cancer After Postchemotherapy Retroperitoneal Lymph Node Dissection With Viable Residual Cancer

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Purpose: No consensus exists on the management of men with nonseminoma and viable nonteratomatous germ cell tumor in the postchemotherapy retroperitoneal lymph node dissection (pcRPLND) specimen after first-line chemotherapy. We analyzed surveillance versus different adjuvant chemotherapy regimens and the influence of time to pcRPLND on oncologic outcomes.

Methods: Data on 117 men treated with cisplatin-based first-line chemotherapy between 1990 and 2018 were collected from 13 institutions. All patients had viable nonteratomatous germ cell tumor in the pcRPLND specimen. Surgery was performed after a median of 57 days, followed by either surveillance (n = 64) or adjuvant chemotherapy (n = 53). Primary end points were progression-free survival (PFS), cancer-specific survival (CSS), and overall survival (OS).

Results: After controlling for International Germ Cell Cancer Cooperative Group risk group and percent of viable malignant cells found at RPLND, no difference was observed between men managed with surveillance or adjuvant chemotherapy regarding PFS (hazard ratio [HR], 0.72 [95% CI, 0.32 to 1.6]; P = .4), CSS (HR, 0.69; 95% CI, 0.20 to 2.39; P = .6), and OS (HR, 0.78 [95% CI, 0.25 to 2.44]; P = .7). No statistically significant differences for PFS, CSS, or OS were observed on the basis of chemotherapy regimen or in men treated with pcRPLND ≤57 versus >57 days after first-line chemotherapy. Residual disease with <10% versus ≥10% viable cancer cells were associated with a longer PFS (HR, 3.22 [95% CI, 1.29 to 8]; P = .012). Relapse in the retroperitoneum was observed in 34 (29%) men.

Conclusion: Men with a complete resection at pcRPLND and <10% viable cells have favorable outcomes without further treatment. Complete retroperitoneal resection seems more important than early pcRPLND.

Amiri A, Krumpolec P, **Mego M**, Ukropcová B, **Chovanec M**, Ukropec J.

Habitual physical activity modulates cardiometabolic health in long-term testicular cancer survivors

Support Care Cancer. 2023 Aug 26;31(9):539.

Purposes: Physical activity (PA) may mitigate late cardiometabolic toxicity of cisplatin-based chemotherapy

in testicular germ cell tumor (TGCT) long-term survivors. In this cross-sectional study, we evaluated the effects of habitual PA on metabolic syndrome (MetS) prevalence, and on the markers of cardiometabolic health and chronic inflammation in a population of long-term TGCT survivors.

Methods: MetS prevalence was evaluated, and habitual PA was assessed using Baecke's habitual PA questionnaire in TGCT survivors (n=195, age=41.1±8.1years, 11.7±5.2years post-therapy) and healthy male controls (n=41, age=38.2±8.8years). Participants were stratified into low- and high-PA groups based on median values. Differences were examined between low- and high-PA groups (in the entire sample, TGCT survivor sub-samples differing in disease stage, and healthy controls), and between TGCT survivors and controls. Next, TGCT survivors were stratified into age- and BMI-matched sub-groups based on post-treatment time (5-15/15/30years) and number of chemotherapy cycles (≤ 3 / > 3), allowing us to detect age- and BMI-independent effects of habitual PA on cardiometabolic health in the given TGCT survivor sub-populations. A correlation matrix of habitual PA and sport activity with cardiometabolic and pro-inflammatory markers was generated.

Results: TGCT survivors had higher MetS prevalence than controls. Patients with high habitual PA had lower waist circumference and Systemic Inflammation Index. Habitual PA scores correlated positively with HDL-cholesterol and negatively with waist circumference and atherogenic risk. Furthermore, cardiometabolic benefits of habitual PA were more pronounced in patients with disease stages 1 and 2. Effects of habitual PA on patients sub-populations stratified by chemotherapy dose and post-treatment time clearly showed that higher levels of habitual PA were associated with lower numbers of

MetS components, except for patients who received more than 3 chemotherapy cycles and were examined more than 15 years post-therapy.

Conclusions: Higher levels of habitual PA effectively mitigated cardio-metabolic toxicity in TGCT survivors. Patients with higher cumulative doses of chemotherapy may need structured exercise interventions involving higher-intensity physical activity to achieve significant improvements in cardiometabolic health.

INÉ

Chalova P, Tazky A, Skultety L, Minichova L, Chovanec M, Ciernikova S, Mikus P, Piestansky J.

Determination of short-chain fatty acids as putative biomarkers of cancer diseases by modern analytical strategies and tools: a review

Front Oncol. 2023 Jun 27;13:1110235.

Short-chain fatty acids (SCFAs) are the main metabolites produced by bacterial fermentation of non-digestible carbohydrates in the gastrointestinal tract. They can be seen as the major flow of carbon from the diet, through the microbiome to the host. SCFAs have been reported as important molecules responsible for the regulation of intestinal homeostasis. Moreover, these molecules have a significant impact on the immune system and are able to affect inflammation, cardiovascular diseases, diabetes type II, or oncological diseases. For this purpose, SCFAs could be used as putative biomarkers of various diseases, including cancer. A potential diagnostic value may be offered by analyzing SCFAs with the use of advanced analytical approaches such as gas chromatography (GC), liquid chromatography (LC), or capillary electrophoresis (CE) coupled with mass spectrometry (MS). The presented review summarizes the importance of analyzing SCFAs from clinical and analytical perspective. Current advances in

the analysis of SCFAs focused on sample pretreatment, separation strategy, and detection methods are highlighted. Additionally, it also shows potential areas for the development of future diagnostic tools in oncology and other varieties of diseases based on targeted metabolite profiling.

Abstrakty z konferencií

Scepanovic D, Masarykova A, Fekete M, Hanicova A, Dolinska Z, Povinec P.

Correlation of quantified metabolic activity with Gross Tumor Volume in patients with Non Small Cell Lung Cancer.

IASLC 2023 World Conference on Lung Cancer | Singapore (WCLC 2023)

Mego M, Danis R, Chovanec J, Jurisova S, Bystricky B, Porsok S, Konkolovsky P, Vaclav V, Wagnerova M, Stresko M, Brezinova B, Reckova M, Sutekova D, Pazderova N, Novisedlakova M, Zomborska E, Ciernikova S, Svetlovska D, Drgona L.

Randomized double-blind, placebo-controlled multicenter phase III study of prevention of irinotecan-induced diarrhea by a probiotic mixture containing Bifidobacterium, BB-12 and Lactobacillus rhamnosus, LGG in colorectal cancer patients: The Probio SK 006-Slovak Cooperative Oncology Group trial.

J Clin Oncol 41, 2023 (suppl 16; abstr e24109)

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

Chemotherapy induced peripheral neuropathy (CIPN) and biomarkers of gut microbial translocation in long-term survivors of testicular germ cell tumors.

J Clin Oncol 41, 2023 (suppl 16; abstr e17032)