Long-term toxicity of cisplatin in germ-cell tumor survivors

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Objectives: To systematically evaluate evidence regarding the long-term toxicity of cisplatin in GCT survivors.

Methods: We conducted a systematic review of PubMed/Medline in February 2017 according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. Identified reports were reviewed according to the Consolidated Standards of Reporting Trials (CONSORT) criteria. Eighty-three studies were selected for inclusion in this analysis. Evidence synthesis: Included reports evaluated long-term toxicities of cisplatin-based chemotherapy in GCT survivors. Studies reporting neuro- and ototoxicity, secondary malignancies, cardiovascular, renal and pulmonary toxicities, hypogonadism and infertility were found. Seven studies (8%) reported genetic underpinnings of long-term toxicities and 14 (19%) studies correlated long-term toxicities with circulating platinum levels and cumulative dose of cisplatin, respectively. Significant risks for long-term toxicities associated with cisplatin and platinum-based regimens were reported. The cumulative dose of cisplatin and circulating platinum were reported as risk factors. Several single-nucleotide polymorphisms identified patients susceptible to cisplatin compared with wild-type individuals.

Results: With a median follow-up of 4.4 years, patients with good, intermediate, and poor risk disease by IGCCCG criteria treated at IU had 5-year PFS of 90%, 84%, and 54% and 5-year OS of 97%, 92%, and 73% respectively. The 5-year PFS for all patients in the IU cohort was 79% (95%CI, 76% to 82%). The 5-year OS for the IU cohort was 90% (95% CI, 87% to 92%). IU testis cohort had 5-year OS 94% (95% CI, 91% to 96%) vs. 75% (95% CI, 73% to 78%) for the SEER “distant” cohort between 2000-2014. P-value <0.0001.

Conclusion: The MDC approach to GCT at high-volume cancer center associated with improved overall survival outcomes in this contemporary dataset. OS is significantly higher in the IU cohort compared to the IGCCCG and SEER “distant” cohort.

KARCINÓM PRSNÍKA


Down-regulation of traditional oncomiRs in plasma of breast cancer patients


Deregulated expression of microRNAs has the oncogenic or tumor suppressor function in cancer. Since miRNAs in plasma are highly stable, their quantification could contribute to more precise cancer diagnosis, prognosis and therapy prediction. We have quantified expression of seven oncomiRs, namely miR-17/92 cluster (miR-17, miR-18a, miR-19a and miR-20a), miR-21, miR-27a and miR-155, in plasma of 137 breast cancer (BC) patients. We detected down-regulation of six miRNAs in patients with invasive BC compared to controls; however, only miR-20a and miR-27a down-regulations were statistically significant.
Comparing miRNA expression between early and advanced stages of BC, we observed statistically significant decrease of miR-17 and miR-19a. We identified down-regulation of miR-17 and miR-20a in patients with clinical parameters of advanced BC (lymph node metastasis, tumor grade 3, circulating tumor cells, higher Ki-67-related proliferation, hormone receptor negativity and HER2 amplification), when compared to controls. Moreover, decreased level of miR-17 was found from low to high grade. Thus, miR-17 could represent an indicator of advanced BC. Down-regulated miR-27a expression levels were observed in all clinical categories regardless of tumor progression. Hence, miR-27a could be used as a potential diagnostic marker for BC. Our data indicates that any changes in miRNA expression levels in BC patients in comparison to controls could be highly useful for cancer-associated pathology discrimination. Moreover, dynamics of miRNA expression changes could be used for BC progression monitoring.

**GASTROINTESTINALNE MALIGNITY**


 Patients with CCSA were randomized 1:1 to placebo or 6 mg of pegfilgrastim ~24 hours after receiving chemotherapy plus bevacizumab every 14 days. The study population included 4 cycles, but patients could continue treatment for ≤ 60 months. The primary endpoint was incidence of grade 3/4 FN in the first 4 cycles. The secondary endpoints included the objective response rate (ORR), overall survival, and progression-free survival, analyzed at the end of the long-term follow-up period.

**Results:** A total of 845 patients were randomized from November 2009 to January 2012 (422, pegfilgrastim; 423, placebo). Pegfilgrastim significantly reduced the incidence of grade 3/4 FN in the first 4 treatment cycles (pegfilgrastim, 2.4%; 95% confidence interval [CI], 1.1%-4.3%; placebo, 5.7%; 95% CI, 3.7%-8.3%; odds ratio [OR], 0.41; P = .014). No significant differences were observed between the 2 arms in ORR (OR, 1.15; P = .330), overall survival (hazard ratio, 0.94; P = .440), and progression-free survival (hazard ratio, 0.93; P = .300).

**Conclusion:** Pegfilgrastim reduced the FN incidence in patients with advanced CRC receiving chemotherapy and bevacizumab. Administration of pegfilgrastim was tolerable and did not negatively affect the tumor response or survival in this patient population.

**SARKÓMY**


**Background:** Pegfilgrastim’s role in reducing the risk of febrile neutropenia (FN) in patients with colorectal cancer (CRC) receiving chemotherapy plus bevacizumab was not previously evaluated in a prospective study. The present phase III, double-blind trial evaluated the efficacy of pegfilgrastim versus placebo in reducing the incidence of grade 3/4 FN in patients with advanced CRC receiving bevacizumab combined with first-line chemotherapy (FOLFOX [leucovorin, 5-fluorouracil, oxaliplatin] or FOLFIRI [leucovorin, 5-fluorouracil, irinotecan]).

**Patients and methods:** Patients aged ≥ 18 years with locally advanced or metastatic CRC were randomized 1:1 to placebo or 6 mg of pegfilgrastim—24 hours after receiving chemotherapy plus bevacizumab every 14 days. The study treatment period included 4 cycles, but patients could continue treatment for ≤ 60 months. The primary endpoint was incidence of grade 3/4 FN in the first 4 cycles. The secondary endpoints included the objective response rate (ORR), overall survival, and progression-free survival, analyzed at the end of the long-term follow-up period.

**Results:** A total of 845 patients were randomized from November 2009 to January 2012 (422, pegfilgrastim; 423, placebo). Pegfilgrastim significantly reduced the incidence of grade 3/4 FN in the first 4 treatment cycles (pegfilgrastim, 2.4%; 95% confidence interval [CI], 1.1%-4.3%; placebo, 5.7%; 95% CI, 3.7%-8.3%; odds ratio [OR], 0.41; P = .014). No significant differences were observed between the 2 arms in ORR (OR, 1.15; P = .330), overall survival (hazard ratio, 0.94; P = .440), and progression-free survival (hazard ratio, 0.93; P = .300).

**Conclusion:** Pegfilgrastim reduced the FN incidence in patients with advanced CRC receiving chemotherapy and bevacizumab. Administration of pegfilgrastim was tolerable and did not negatively affect the tumor response or survival in this patient population.

**ABSTRAKY PRÍSPEVKOV ZO ZAHRAŠIČNÝCH KONFERENCIÍ**

**KARCÍNOM PLÚC**

Masarykova A, Scepanovic D, Bires P, Lederleitner D, Pobijakova M, Povinpec P

The differences between two groups of patients with non small cell lung cancer depending on the imaging for radiotherapy planning ESTRO 36, Vienna, Austria, 5-9 May 2017 (poster: PO-0667)

**GASTROINTESTINÁLNE MALIGNITY**

Masarykova A, Zavacka I, Scepanovic D, Dzongov M, Pohrancova M, Dolinska Z, Pobijakova M

Relationship between the site of esophageal carcinoma and survival of patients with locally advanced disease ESMO 19th World Congress on Gastrointestinal Cancer, 28 June – 1 July 2017, Barcelona, Spain (poster: P-053)

Masarykova A, Dzongov M, Haniecova A, Zavacka I, Scepanovic D

Combined modality therapy for naso-oropharyngeal solitary extramedullary plasma cytoma – case report International Journal of Otorhinolaryngology and Head and Neck Surgery (accepted)

HEMATOLOGICKÉ MALIGNITY