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KARCINÓM PRSNÍKA

Mego M, Karaba M, Minarik G, Benca J, Sedlackova T, Tothova L, Vlkova B, Cierna Z, Janega P, Luha J, Gronesova P, Pindak D, Fridrichova I, Celec P, Reuben JM, Cristofanilli M**, Mardiak J.**

Relationship between circulating tumor cells, blood coagulation and urokinase-plasminogen-activator system in early breast cancer patients.

The Breast Journal, 2014 (In press)

Cancer is a risk factor for venous thromboembolism (VTE) and plasma d-dimer (DD) and tissue factor (TF) are established VTE associated markers. Circulating tumor cells (CTCs) are associated with the risk of VTE in metastatic breast cancer. This study aimed to correlate CTCs, blood coagulation and the urokinase-plasminogen-activator (uPA) system in primary breast cancer (PBC) patients. This prospective study included 116 PBC patients treated by primary surgery. CTCs were detected by quantitative RT-PCR assay for expression of epithelial (CK19) or epithelial-mesenchymal transition (EMT) genes (TWIST1, SNAIL1, SLUG, ZEB1, FOXC2). Plasma DD, TF, uPA system proteins were detected by ELISA, while expressions of uPA system in surgical specimens were evaluated by immunohistochemistry. CTCs were detected in 27.6% patients. Patients with CTCs had a significantly higher mean plasma DD (ng/mL) than those of patients without CTCs (632.4 vs. 365.4, p=0.000004). There was no association between plasma TF and CTCs. Epithelial CTCs exhibit higher expression of uPA system genes compared to EMT_CTCs. Patients with CTCs had higher plasma uPA proteins than those of patients without CTCs; there was no correlation between tissue expression of uPA system, CTCs, DD or TF levels. In multivariate analysis CTCs and patients age were independent factors associated with plasma DD. We found association between plasma DD and CTCs indicating a potential role for activation of the coagulation cascade in the early metastatic process. CTCs could be directly involved in coagulation activation or increased CTCs could be marker of aggressive disease and increased VTE risk.

Giuliano M, Giordano A, Jackson S, De Giorgi U, **Mego M**, Cohen EN, Gao H, Anfossi S, Handy BC, Ueno NT, Alvarez RH, De Placido S, Valero V, Hortobagyi GN, Reuben JM, Cristofanilli M.

Circulating tumor cells as early predictors of metastatic spread in breast cancer patients with limited metastatic dissemination.

Breast Cancer Res. 2014 Sep 16;16(5):440.

IntroductionTraditional factors currently used for prognostic stratification do not always predict adequately treatment response and disease evolution in advanced breast cancer patients. Therefore, the use of blood-based markers, such as circulating tumor cells (CTCs), represents a promising complementary strategy for disease monitoring. In this retrospective study, we explored the role of CTC counts as predictors of disease evolution in breast cancer patients with limited metastatic disseminaion. Methods492 advanced breast cancer patients who had a CTC count assessed by CellSearch prior to starting a new line of systemic therapy were eligible for this analysis. Using the threshold of 5 cells/7.5 mL of blood, pretreatment CTC counts were correlated in the overall population with metastatic site distribution, evaluated at baseline and at the time of treatment failure, using the Fisher¿s Exact test. Time to visceral progression, as well as, time to the development of new metastatic lesions and sites were estimated in patients with non-visceral metastases and with single-site metastatic disease, respectively, by the Kaplan-Meier method. Survival times were compared among groups according to pretreatment CTC count by log-Rank test.ResultsIn the overall population, pretreatment CTCs¿¿¿5 were associated with increased baseline number of metastatic sites, compared with CTCs¿<¿5 (p¿=¿.0077). At the time of treatment failure, patients with CTCs¿¿¿5 developed more frequently new metastatic lesions and sites compared to those with CTCs <5 (development of new lesions p¿=¿.0002; development of new sites p¿=¿.0031). Among patients with disease originally confined to non-visceral sites, CTCs¿¿¿5 were associated with remarkably shorter time to visceral metastases (p¿=¿.0021) and overall survival (p¿=¿.0006),compared with CTCs¿<¿5. Finally, in patients with single-site metastatic disease, CTCs¿¿¿5 were associated with a significant reduction of the time to development of new metastatic sites (p¿=¿.0051) and lesions (p¿=¿.0002), and with worse overall survival (p¿=¿.0101). Conclusion. Our results suggest that baseline CTC counts can be used as an early predictor of metastatic potential in breast cancer patients with limited metastatic dissemination.

Rordorf T, Hassan AA, Azim H, Alexandru E, Er O, Gokmen E, Güral Z, **Mardiak J,** Minchev V, Peintinger F, Szendroi M, Takac I, Tesarova P, Vorobiof D, Vrbanec D, Yildiz R, Yücel S, Zekri J, Oyan B.

Bone health in breast cancer patients: A comprehensive statement by CECOG/SAKK Intergroup.

Breast. 2014 (In press)

Bone is the most common site of distant metastases in breast cancer that can cause severe and debilitating skeletal related events (SRE) including hypercalcemia of malignancy, pathologic fracture, spinal cord compression and the need for palliative radiation therapy or surgery to the bone. SRE are associated with substantial pain and morbidity leading to frequent hospitalization, impaired quality of life and poor prognosis. The past 25 years of research on the pathophysiology of bone metastases led to the development of highly effective treatment options to delay or prevent osseous metastases and SRE. Management of bone metastases has become an integral part of cancer treatment requiring expertise of multidisciplinary teams of

medical and radiation oncologists, surgeons and radiologists in order to find an optimal treatment for each individual patient. A group of international breast cancer experts attended a Skeletal Care Academy Meeting in November 2012 in Istanbul and discussed current preventive measures and treatment options of SRE, which are summarized in this evidence-based consensus for qualified decision- making in clinical practice.

ABSTRAKTY A POSTERY ZO ZAHRANIČNÝCH KONFERENCIÍ

KARCINÓM PRSNÍKA

Prednáška:

Mego M, Gao H, Cohen EN, Anfossi S, Giordano A, Sanda T, Fouad TM, **Sevcikova K,** Woodward WA, Alvarez RH, Valero V, Ueno NT, Hortobagyi GN, Cristofanilli M, Reuben JM.

Myeloid-derived dendritic cells have reduced ability to produce IL-12 and TNF-α in inflammatory breast cancer (IBC) patients with ≥5 circulating tumor cells (CTC).

Advances in Circulating Tumor Cells (ACTC): From Basic Research to Clinical Practice. October 8th –11th, 2014, Crete, Greece