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Onkológia (Bratisl.), 2015; roč. 10(4): 264–265

KARCINÓM PRSNÍKA

Mego M, Cierna Z, Janega P, Karaba M, Minarik G, Benca J, Sedláckova T, Sieberova G, Gronesova P, Manasova D, Pindak D, Sufliarsky J, Danihel L, Reuben JM, Mardiak J.

Relationship between circulating tumor cells and epithelial to mesenchymal transition in early breast cancer

BMC Cancer. 2015 Jul 22;15:533.

Background: Circulating tumor cells (CTCs) play a crucial role in tumor dissemination and are an independent survival predictor in breast cancer (BC) patients. Epithelial to mesenchymal transition (EMT) is involved in cancer invasion and metastasis. The aim of this study was to assess correlation between CTCs and expression of EMT transcription factors TWIST1 and SLUG in breast tumor tissue.

Methods: This study included 102 early BC patients treated by primary surgery. Peripheral blood mononuclear cells (PBMC) were depleted of hematopoietic cells using RosetteSep™ negative selection kit. RNA extracted from CD45-depleted PBMC was interrogated for expression of EMT (TWIST1, SNAIL1, SLUG, FOXC2 and ZEB1) and epithelial (KRT19) gene transcripts by qRT-PCR. Expression of TWIST1 and SLUG in surgical specimens was evaluated by immunohistochemistry and quantified by multiplicative score.

Results: CTCs were detected in 24.5 % patients. CTCs exhibiting only epithelial markers were present in 8.8 % patients, whereas CTCs with only EMT markers were observed in 12.8 % of pts and CTCs co-expressing both markers were detected in 2.9 % pts. We observed lack of correlation between CTCs and expression of TWIST1 and SLUG in breast cancer cells or cancer associated stroma. Lack of correlation was observed for epithelial CTCs as well as for CTCs with EMT.

Conclusions: In this translational study, we showed a lack of association between CTCs and expression of EMT-inducing transcription factors, TWIST1 and SLUG, in breast tumor tissue. Despite the fact that EMT is involved in cancer invasion and metastasis our results suggest, that expression of EMT proteins in unselected tumor tissue is not surrogate marker of CTCs with either mesenchymal or epithelial features.

Cohen EN, Gao H, Anfossi S, **Mego M**, Reddy NG, Debeb B, Giordano A, Tin S, Wu Q, Garza RJ, Cristofanilli M, Mani SA, Croix DA, Ueno NT, Woodward WA, Luthra R, Krishnamurthy S, Reuben JM

Inflammation mediated metastasis: immune induced epithelial-to-mesenchymal transition in inflammatory breast cancer cells
PLoS One. 2015 Jul 24;10(7):e0132710.

Inflammatory breast cancer (IBC) is the most insidious form of locally advanced breast cancer; about a third of patients have distant metastasis at initial staging. Emerging evidence suggests that host factors in the tumor microenvironment may interact with underlying IBC cells to make them aggressive. It is unknown whether immune cells associated to the IBC microenvironment play a role in this scenario to transiently promote epithelial to mesenchymal transition (EMT) in these cells. We hypothesized that soluble factors secreted by activated immune cells can induce an EMT in IBC and thus promote metastasis. In a pilot study of 16 breast cancer patients, TNF- α production by peripheral blood T cells was correlated with the detection of circulating tumor cells expressing EMT markers. In a variety of IBC model cell lines, soluble factors from activated T cells induced expression of EMT-related genes, including FN1, VIM, TGM2, ZEB1. Interestingly, although IBC cells exhibited increased invasion and migration following exposure to immune factors, the ex-

pression of E-cadherin (CDH1), a cell adhesion molecule, increased uniquely in IBC cell lines but not in non-IBC cell lines. A combination of TNF- α , IL-6, and TGF- β was able to recapitulate EMT induction in IBC, and conditioned media preloaded with neutralizing antibodies against these factors exhibited decreased EMT. These data suggest that release of cytokines by activated immune cells may contribute to the aggressiveness of IBC and highlight these factors as potential target mediators of immune-IBC interaction.

GENITOURINÁRNE MALIGNITY

Vrdoljak E, Gore M, Leyman S, Szczylik C, Kharkevich G, Schöffski P, Torday L, **Mardiak J**, Zhang K, Sajben P, Sella A.

Bisphosphonates in patients with renal cell carcinoma and bone metastases: a sunitinib global expanded-access trial subanalysis
Future Oncol. 2015 Jun 29;1-10.

Aim: To investigate retrospectively the effects of bone metastases and bisphosphonates in sunitinib-treated metastatic renal cell carcinoma patients.

Patients & methods: Patients in Groups (Gp) 1 and 2, but not Gp3, had bone metastases. Gp2 received bisphosphonates following standard practice.

Results: Gp2 had less favorable prognosis than Gp1. Gp3 had fewer metastases and the best prognosis. More serious adverse events occurred in Gp2 versus Gp1. The difference in overall survival between Gp1 and Gp2 was not significant after adjusting for covariates. Significantly shorter overall survival in Gp1 versus Gp3 persisted after adjusting for covariates.

Conclusions: Bone metastases may have a negative prognostic impact in metastatic renal cell carcinoma. Bisphosphonates may have delayed early disease progression for prognostically worse sunitinib/bisphosphonate-treated patients.

PREDNÁŠKY A POSTERY ZO ZAHRANIČNÝCH KONFERENCIÍ

KARCINÓM PRSNÍKA

Michal Mego, Silvia Cingelova, Zuzana Cierna, Dana Cholujova, Pavol Janega, Marian Karaba, Paulina Gronesova, Juraj Benca, Tomas Minarik, Viera Labudova, Daniel Pindak, Jozef Sufliarsky, Jozef Mardiak

Correlation between CD3+ tumor infiltrating lymphocytes and plasma cytokines in primary breast cancer patients

J Clin Oncol 33, 2015 (suppl; abstr e22103), ASCO 2015

Branislav Bystricky, Marian Karaba, Juraj Benca, Ludmila Vavrova, Jan Markus, Michal Konecny, Daniel Pindak, Jozef Sufliarsky, Jozef Mardiak, Michal Mego

Heterogeneity of circulating tumor cells in primary breast cancer patients

J Clin Oncol 33, 2015 (suppl; abstr e22037), ASCO 2015

GENITOURINÁRNE MALIGNITY

Michal Mego, Daniela Svetlovska, Vera Miskovska, Jana Obertova, Peter Zuzak, Patrik Palacka, Jan Rajec, Zuzana Sycova-Mila, Michal Chovanec, Maria Reckova, Katarina Rejlekova, Dalibor Ondrus, Stanislav Spanik, Jozef Mardiak

Phase II study of everolimus (E) in refractory testicular germ cell tumors (TGCTs)

J Clin Oncol 33, 2015 (suppl; abstr e15567), ASCO 2015

Michal Chovanec, Michal Mego, Dana Cholujova, Paulina Gronesova, Vera Miskov-

ska, Zuzana Sycova-Mila, Vanda Usakova, Daniela Svetlovska, Peter Bujdak, Stanislav Spanik, Dalibor Ondrus, Jozef Mardiak

A cytokine and angiogenic factor (CAF) analysis in plasma in testicular germ cell tumor patients (TGCTs)

J Clin Oncol 33, 2015 (suppl; abstr e15552), ASCO 2015

Patrik Palacka, Jarmila Kucharska, Michal Mego, Jan Luha, Zuzana Sumbalova, Daniela Svetlovska, Katarina Rejlekova, Jozef Mardiak, Anna Gvozdjakova

Novel prognostic factors in metastatic urothelial carcinoma (MUC)

J Clin Oncol 33, 2015 (suppl; abstr e15525), ASCO 2015

Daniela Svetlovska, Vera Miskovska, Dana Cholujova, Jan Luha, Patrik Palacka, Vanda Usakova, Jana Obertova, Zuzana Sycova-Mila, Michal Chovanec, Jan Rajec, Bibiana Vertakova-Krakovska, Paulina Gronesova, Peter Bujdak, Dalibor Ondrus, Stanislav Spanik, Jozef Mardiak, Michal Mego

Prognostic value of plasma cytokines in metastatic testicular germ cell tumors (TGCTs)

J Clin Oncol 33, 2015 (suppl; abstr e15558), ASCO 2015

GASTROINTESTINÁLNE MALIGNITY

Danijela Scepanovic, Andrea Masarykova, Margita Pobijakova, Zuzana Dolinska, Andrea Hurakova, Martina Kolarcikova-Lukacovicova

Sites of local recurrence at rectal cancer patients depending on the type of surgery

11th Conference of the Society of Radiation Oncology, Biology and Physics, 12 - 13 June

2015, Zerotinsky zamek, Novy Jicin, Czech Republic (poster)

Danijela Scepanovic, Margita Pobijakova, Andrea Masarykova, Andrea Hurakova, Martina Kolarcikova-Lukacovicova, Zuzana Dolinska

K-ras mutation as prognostic factor in our patients with rectal cancer

ESMO 17th World Congress on Gastrointestinal Cancer, 1-4 July 2015, Barcelona, Spain (poster)

PLŮČNE MALIGNITY

Andrea Masarykova, Danijela Scepanovic, Pavol Bires, David Lederleirtner, Margita Pobijakova

Correlation between dose volume analysis and clinical findings of acute esophagitis in patients with locoregionally advanced non-small cell lung cancer treated with radiotherapy

Onco Update Europe 2015, 19-20 June 2015, Vienna, Austria (e-poster)

GYNEKOLOGICKÉ MALIGNITY

Andrea Masarykova, Danijela Scepanovic, Marta Fekete, Alexandra Hanicova, Margita Pobijakova

Postoperative External Beam Radiotherapy versus Vaginal Brachytherapy alone in patients with early stages of uterine carcinoma – our experience

18th ECCO - 40th ESMO European Cancer Congress, 25-29 September 2015, Vienna, Austria (poster)