Tecza et al. Hereditary Cancer in Clinical Practice 2015, **13**(Suppl 2):A9 http://www.hccpjournal.com/content/13/S2/A9

MEETING ABSTRACT



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Copper transport system and response to ovarian cancer chemotherapy

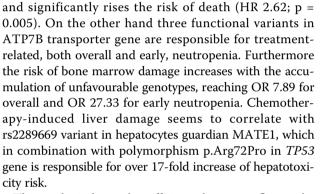
Karolina Tecza^{1*}, Jolanta Pamula-Pilat¹, Zofia Kolosza², Ewa Grzybowska¹

From Annual Conference on Hereditary Cancers 2014 Szczecin, Poland. 25-26 September 2014

Copper is the trace element essential for the proper functioning of the cells because of its role as cofactor of many crucial enzymes, such as cytochrome c oxidase, superoxide dismutase and lysyl oxidase. Cellular transport system ensures the exact distribution of copper throughout the body and consequently its malfunction could lead to serious medical conditions, such as Menkes and Wilson disease. Apart from copper transport this system is used to move platinum and its derivates through the cell and body- including the widely used chemotherapeutic drug cisplatin. It is therefore believed that polymorphic variants in genes encoding the importer (CTR1) and intracellular exporters *via* the TNG network (ATP7A and ATP7B) could alter the drug availability and its therapeutic concentration. As the result of such alterations cisplatin resistance or oversensitivity could be developed leading to cancer therapy failure and/or serious deterioration of patients' condition. Similar consequences could also be the result of modifications in genes encoding multidrug and toxin extrusion proteins (MATE family). These efflux transporters are not the part of the main copper transport system, but are crucial for efficient elimination of toxins, including copper and platinum drugs, in liver and kidneys.

Impact of genetic polymorphisms in copper transport systems on the response to cancer treatment was analysed in the group of 129 women diagnosed with epithelial ovarian cancer receiving cisplatin-based first-line chemotherapy. For this study we selected 11 functional variants in *CTR1, ATP7A, ATP7B, MATE1* and *MATE2-K* genes.

The results show that decrease of platinum importer *CTR1* expression, as the consequence of intronic rs12686377 variant, leads to platinum-resistant phenotype



The results indicate that efficient platinum influx to the cells is crucial for positive reaction to treatment and patients' longer overall survival. Cisplatin-induced toxicity on the other hand seems to be dependent on the management of the drug's concentration- by both intracellular transport (ATP7B) and extrusion (MATE1) systems.

Acknowledgements

This work was financially supported by Cancer Centre and Institute of Oncology in Gliwice institutional grant- 2013 edition.

Authors' details

¹Center for Translational Research and Molecular Biology of Cancer, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Poland. ²Department of Epidemiology and Silesia Cancer Registry, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Poland.

Published: 26 November 2015

doi:10.1186/1897-4287-13-S2-A9

Cite this article as: Tecza *et al*: Copper transport system and response to ovarian cancer chemotherapy. *Hereditary Cancer in Clinical Practice* 2015 13(Suppl 2):A9.



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^{*} Correspondence: ktecza@io.gliwice.pl

¹Center for Translational Research and Molecular Biology of Cancer, Maria Sklodowska-Curie Memorial Cancer Center and Institute of Oncology, Gliwice Branch, Poland

Full list of author information is available at the end of the article