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Session H. Lung cancer

H39 Genetic polymorphism can help physician choosing the best lung cancer chemotherapy

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Background: Lung cancer is one of the most frequent malignancy with high mortality rate. Non small cell lung cancer (NSCLC) is the most common histological type, representing approximately the 85% of all lung cancers. Platinum-based chemotherapy is the standard of care in the first line treatment for patients with advanced or metastatic NSCLC not carrying a driver mutation. Despite the recent advances, the overall survival (OS) of patients receiving chemotherapy remains exiguous, of approximately 8-10 months, with an high rate of toxicities. The new direction in personalization of care is to guarantee the best treatment, both in terms of outcome, and toxicities control. Therefore, the aim of our study is to identify some markers associated with toxicity, through the analysis of genetic polymorphisms involved in drugs metabolism.

Material and methods: We studied 41 chemo-naïve adult patients, with ECOG Performance Status 0-2, affected by NSCLC of all stages, underwent treatment with platinum-doublets, planned for at least 3 cycles. Through a peripheral venous blood sampling we genotyped them for selected polymorphisms using real-time PCR. We characterized Single Nucleotide Polymorphisms (SNPs) involved in detoxification (GSTP1), DNA repair (XRCC1, ERCC1), metabolism of anticancer agents (CYP3A4, CYP3A5, TSER, MTHFR, CYP2C9, CYP1A2, CYP2D6, UGT1A1) and in trans-membrane transport (ABCB1). The statistical analysis was conducted by MINITAB 16.2.3 software. A value of $p < 0.05$ was considered statistically significant.

Results: Toxicities and polymorphisms were prospectively evaluated in 41 patients (33 males and 8 females). Median age of patients was 66,6 (range 33-82). The statistical analysis showed a trend of greater toxicity in patients with polymorphisms leading to reduced metabolism, transport and DNA repair activity. Patient with lower detoxification capacity (homozygous genotype for GSTP1 A313G) showed a greater number of dose-limiting toxicity events ($p = 0.17$).

Conclusions: In this study we indentified an association with genetic polymorphisms and toxicities in NSCLC patients treated with platinum doublets. A larger cohort of patients must be investigated, in order to better understand the role of polymorphisms and to identify a signatures differentiating patients at higher or lower risk of toxicities and relative efficacy of platinum-based chemotherapy.