PLATINUM-BASED CHEMOTHERAPY IN NON-SMALL CELL LUNG CANCER

Background and importance

Platinum-based doublet chemotherapy is the standard treatment for non-small cell lung cancer (NSCLC) for EGFR wild type patients, which presents high percentages of severe adverse events, such nephrotoxicity (20-30%).

Nephrotoxicity is characterized for high morbidity and mortality. Cisplatin is one of the major causes of nephrotoxicity.

The aim of this study was evaluated the influence of CYP27B1 and CYP2R1 gene polymorphisms on nephrotoxicity due to platinum-based chemotherapy in non-small cell lung cancer.

Material and methods


CYP27B1 (rs4646536, rs3782130, rs703842, rs10877012) and CYP2R1 (rs10741657) polymorphisms were analyzed by real-time PCR using TaqMan® probes. Nephrotoxicity was evaluated according to the Common Terminology Criteria for Adverse Events (CTCAE) v.4.0.

Conclusions and relevance

Our results suggest that rs4646536, rs3782130, rs703842, and rs10877012 influence nephrotoxicity in platinum-based chemotherapy. CYP27B1 is the only enzyme capable of activating vitamin-D. Therefore, genetic study of these polymorphisms could be used as a toxicity prediction biomarker in NSCLC patients going under based platinum chemotherapy.

Results

Patients median age at NSCLC diagnosis was 62[53-67] years; 73.3% (121/165) men; 69.09% (114/165) stage IIIB-V; 59.39% (98/165) adenocarcinoma; 58.18% (96/165) family history of cancer; 24.24% (40/164) Previous lung disease; EGFR status: 10.91% (18/165) Mutated. Chemotherapy agents: 18.29% (30/164) Gemcitabine; 21.34% (35/164) Paclitaxel; 24.39% (40/164); 35.98% (59/164). Nephrotoxicity: 17.58% (29/165).

Patients carrying the CYP27B1-rs4646536 (p=0.0312; OR:0.32; CI95%:0.10-0.84; AG vs AA); CYP27B1-rs3782130 (p=0.0247; OR:0.22; CI95%:0.05-0.85; CC vs G); CYP27B1-rs703842 (p=0.0121; OR:0.15; CI95%:0.03-0.67; CT vs CC) and CYP27B1-rs10877012 (p=0.0239; OR:4.50; CI95%:1.17-17.2; TT vs G), were associated with nephrotoxicity.

However, for CYP2R1-rs10741657 we did not find a statistically significant association.

References