INFLUENCE OF GENETIC VARIANTS IN THE VITAMIN D HYDROXYLATION PATHWAY AS A RESPONSE FACTOR TO PLATINUM-BASED CHEMOTHERAPY IN NONSMALL CELL LUNG CANCER

L.E. PINEDA LANCHEROS[1],J.M. GÁLVEZ NAVAS[1,3], C. PÉREZ RAMÍREZ[1,3], M.R. CANTUDO CUENCA[4], A. JIMÉNEZ MORALES[4]

[1]PHARMACOGENETICS UNIT. PHARMACY SERVICE, UNIVERSITY HOSPITAL VIRGEN DE LAS NIEVES, GRANADA, SPAIN.
[2]PHARMACY SERVICE, UNIVERSITY HOSPITAL VIRGEN DE LAS NIEVES, GRANADA, SPAIN.
[3]DEPARTMENT OF BIOCHEMISTRY AND MOLECULAR BIOLOGY II,
INSTITUTE OF NUTRITION AND FOOD TECNOLOGY "JOSÉ MATAIX", BIOMEDICAL RESEARCH CENTER,
UNIVERSITY OF GRANADA, GRANADA, SPAIN.

lepinedal@correo.ugr.es

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Background and importance

Chemotherapy based on platinum compounds is the standard treatment for non-small cell lung cancer (NSCLC) patients with EGFR wild type and is also used as second line in mutated EGFR patients.

Vitamin-D may influence chemotherapy response by inhibiting tumor progression, suppressing metastasis, cell proliferation, and angiogenesis, or promoting apoptosis.

Therefore, **gene polymorphisms vitamin-D** signalling pathway might have an impact on chemotherapy response. Recent studies reported that genetic back-ground plays a key role in the chemotherapy response.

However, little is known about the implication of **CYP2R1** and **CYP27B1 gene polymorphisms**, which regulate the activation of circulating vitamin-D through hydroxylation, in the **response** of platinum based chemotherapy.

Aim and objectives

The aim of this study was to evaluate the influence of polymorphisms in the CYP2R1 and CYP27B1 genes on the platinum based chemotherapy response in patients with NSCLC.

Material and methods

A

A prospective cohorts study was conducted. 165 patients diagnosed with NSCLC between 2003-2019, followed-up until December 2020.

B

CYP27B1 (rs4646536, rs3782130, rs703842, rs10877012) and *CYP2R1* (rs10741657) polymorphisms were analyzed by real-time PCR using TaqMan® probes.

C

Response (CR: complete response, PR: partial response) and no response (SD: stable disease, PD: progressive disease) were evaluated.

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% (40/165) Previous lung disease; EGFR status: 52.73% (87/165) Wild type, 10.91% (18/165) Mutated, 36.36% (18/165) Unknown; 22.56% Surgery; 31.52% Radiotherapy; Chemotherapy agents: 18.29% (30/164) Gemcitabine; 21.34% (35/164) Paclitaxel; 24.39% (40/164); 35.98% (59/164). 65.85% (108/164) response; 34.15% (56/164) no response.

Patients carrying the CYP2R1-rs10741657-G alleles were associated with better response (p=0.017; OR: 3.17; 95% CI: 1.19-8.42; G vs AA). However, for CYP27B1 (rs4646536, rs3782130, rs703842, rs10877012) we did not find a statistically significant association.

Conclusion and relevance

Our results suggest that CYP2R1 rs10741567 G-allele influences response in platinum-based chemotherapy in NSCLC patients. Therefore, this polymorphism could be used as a response biomarker in NSCLC patients in treatment with platinum based chemotherapy.

References: Xiong L, Cheng J, Gao J, Wang J, Liu X, Wang L. Vitamin D receptor genetic variants are associated with chemotherapy response and prognosis in patients with advanced non-small-cell lung cancer. Clin Lung Cancer. 2013 Jul;14(4):433-9. doi: 10.1016/j.cllc.2013.01.004. Epub 2013 Mar 22. PMID: 23522953.