

## Genetic polymorphisms of drug transporters are associated with tumor response and toxicities in NSCLC pts receiving docetaxel containing chemotherapy

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**Background:** Docetaxel (Taxotere<sup>®</sup>) has been known as one of the most active anti-cancer drugs for breast, ovary, head and neck, prostate, and NSCLC. Neutropenia and asthenia are the toxic reactions frequently observed during docetaxel treatment. We carried out the association study between docetaxel-related toxicities, tumor response and genetic polymorphisms of CYP3A4, CYP3A5, ABCB2, and SLCO1B3. **Method:** Clinical information was collected from 54 advanced or metastatic NSCLC patients who received docetaxel containing chemotherapy. We extracted genomic DNA from peripheral blood and genotyped CYP3A4 (CYP3A4\*1B, CYP3A4\*18, CYP3A4\*3), CYP3A5 (CYP3A5\*2, CYP3A5\*3), ABCB1 (C1236T, G2677T/A, C3435T), SLCO1B3 (rs11045585), ABCB2 (rs12762549) using direct sequencing and pyrosequencing. **Result:** Mean age was 59.8 (35-78) yrs and M:F ratio was 41:13. Fifty pts (92.6%) were in ECOG performance status 0-1. Fifty three pts (98.1%) were stage III or IV. Forty six pts (85.2%) received more than 60 mg/m<sup>2</sup> of docetaxel. Objective response rate (CR+PR) was 42.6%. Fifteen pts (27.8%) were still in SD and 14 pts (25.9%) showed PD. Severe neutropenia (G3-4) occurred in 33 pts (61.1%). Mild to moderate leukopenia, anemia and thrombocytopenia (G1-2) were observed in 21 (39.8%), 47 (87.0%) and 14 (25.9%) pts. Asthenia occurred in 34 pts (63.0%) and G2-3 asthenia occurred in 19 pts (35.2%). Genetic variants of CYP3A4 (CYP3A4\*1B, CYP3A4\*18, CYP3A4\*3) and CYP3A5\*2 were not found. Statistically significant associations existed between G2677T/A, ABCB2 and severe leukopenia ( $p=0.025$ ,  $p=0.028$ ) as well as between C3435T and neutropenia ( $p=0.029$ ), anemia ( $p=0.044$ ). Significant associations between tumor response and G2677T/A (OR=4.54) and SLCO1B3 (OR=9.44) were observed. **Conclusion:** Taken together, our data suggest that G2677T/A (MDR1) and SLCO1B3 may be major pharmacogenetic predictors for severe hematologic toxicities and tumor response in advanced NSCLC patients receiving docetaxel containing chemotherapy.

## Capecitabine monotherapy, and the clinical significance of neutrophil-lymphocyte ratio vs platelet-lymphocyte ratio in metastatic colorectal Cancer

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**Background:** Oxaliplatin- and irinotecan-based combination chemotherapy with infusional 5-FU and leucovorin are currently the standard therapies for metastatic colorectal cancer. The objectives of this study were to evaluate the efficacy of capecitabine monotherapy as third line therapy for metastatic colorectal cancer after failure of chemotherapy containing oxaliplatin and irinotecan, and to determine whether the neutrophil-lymphocyte ratio (NLR), or the platelet-lymphocyte ratio (PLR) are significant prognostic marker in metastatic colorectal cancer. **Methods:** We analyzed 60 patients with metastatic colorectal cancer who received capecitabine monotherapy after the failure of FOLFOX and FOLFIRI. Capecitabine was administered at 1250 mg/m<sup>2</sup> twice daily for 2 weeks, every 3 weeks. The NLR and PLR were calculated from complete blood counts in baseline laboratory test before the first cycle chemotherapy. **Results:** The overall response rate was 6.7% and stable disease was 41.7%. The disease control rate was 48.3%. The median progression-free survival (PFS) was 2.8 months (95% CI, 1.5-4.1 months) and the median overall survival (OS) was 9.7 months (95% CI, 7.6-11.7 months). The most frequent adverse event was hand-foot syndrome (all-grade 26.6%; grade3 5%). The response of capecitabine, NLR, and PLR were observed as good prognostic markers of OS in univariate analysis ( $p<0.001$ , 0.004, and 0.002, respectively). The response of capecitabine and PLR were independent prognostic marker in multivariate analysis (Hazard ratio 2.757, 95% CI 1.357-5.599,  $p=0.005$  and hazard ratio 2.091, 95% CI 1.231-3.552,  $p=0.006$ , respectively). **Conclusion:** The capecitabine monotherapy showed a moderate disease control and a tolerable toxicity profile as third line treatment for metastatic colorectal cancer. The response of capecitabine and PLR may be simple and useful prognostic index for metastatic colorectal cancer.