ERCC1 EXPRESSION IS ASSOCIATED WITH RESPONSE TO GEMOX PLUS ERLOTINIB IN PANCREATIC ADENOCARCINOMA PATIENTS

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Background: Gemcitabine in combination with erlotinib has been approved for the treatment of metastatic pancreatic cancer. In patients with good performance status, gemcitabine combination chemotherapy, i.e. with oxaliplatin (GEMOX) is commonly being used. Although there is some evidence that GEMOX plus erlotinib is beneficial in a subgroup of patients compared to GEMOX alone in cholangiocellular carcinoma no such data exist for pancreatic cancer. Selecting patients, which might benefit from this regimen, by identifying predictive biomarkers is highly desirable. A candidate biomarker for resistance to platinum based therapies is displayed by excision repair cross complementing rodent repair deficiency, complementation group 1 (ERCC1) overexpression. Thus, we performed this retrospective analysis in unselected patients to investigate the efficacy and safety of this chemotherapy regimen. Response was associated to ERCC1 expression.

Methods: Fifty-one patients with metastatic adenocarcinoma of the pancreas receiving off-protocol GEMOX in combination with erlotinib at a single institution between 2006 and 2012 were included in this analysis. Data collection included baseline demographic, clinical and toxicity data as well as progression-free survival (PFS) and overall survival (OS). Additionally, immunohistochemistry was performed to stain for ERCC1 expression. Samples were assessed and scored by a blinded trained pathologist.

Results: A total of 51 patients were included in this study. The mean age was 62 years, and the median ECOG performance score was 1 (range, 0-1). Clinical response and disease stabilization was achieved in 54% of the patients. The median PFS was 4.4 months (95% CI 4.4-5.4) and median overall survival was 8.5 months (95% CI 6.1-10.9). However, the subgroup of 27 patients, who benefited from this regimen in terms of abrogation of progression, had a PFS of 6.7 and an OS of 11.2 months. Interestingly, these patients had a statistically significant overexpression of ERCC1 (Histoscore 10, p ≤0.05) compared to non-responders (Histoscore 7.2). Myelosuppression was the most frequent side effect. The most common severe nonhematological toxicity was diarrhea (5/51).

Conclusion: These data suggest that the combination of GEMOX plus erlotinib is safe and active in about half of the patients treated with this regimen. Patients, who had a higher ERCC1 staining pattern were most likely to benefit from this therapy. It has been described previously in preclinical models that EGFR inhibition can lead to ERCC1 downregulation, thus re-sensitizing cells to platinum drugs. This effect might contribute to our observations. Prospective biomarker studies are warranted to further confirm these findings.