Relationship Between the Expression of O-Methylguanine-DNA Methyltransferase (MGMT) and p53, and the Clinical Response in Metastatic Pancreatic Adenocarcinoma Treated with FOLFIRINOX

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Résumé en anglais	BACKGROUND: To date, no predictive biomarker for the efficacy of FOLFIRINOX in metastatic pancreatic adenocarcinoma has been demonstrated. Deficiency in O-methylguanine-DNA methyltransferase (MGMT) has been associated with a therapeutic response in endocrine tumors of the pancreas and the lack of expression of protein 53 (p53) could interfere with the action of MGMT. OBJECTIVE: The aim of our study was to assess the prevalence of MGMT and p53 in patients with metastatic pancreatic adenocarcinoma treated with FOLFIRINOX as a first-line treatment and to investigate their association with therapeutic response and survival. PATIENTS AND METHODS: The immunohistochemical expression of MGMT was recorded as present or absent and the expression of p53 was semi-quantitatively scored in 30 patients with metastatic pancreatic adenocarcinoma, at Angers Hospital in France between September 2011 and June 2015. Clinical and radiologic data were collected retrospectively. RESULTS: The presence or absence of MGMT expression entailed no significant differences in response rate. Median values of progression-free survival (PFS) and overall survival (OS) were lower in patients with MGMT expression, but sample size is too small to conclude that there is a statistically significant difference. No significant relationship for response rate and PFS was observed in relation with p53 expression. By contrast, patients with a strong tumor expression of p53 had a significantly lower OS compared to patients with no or weak expression of the protein ($p = 0.027$). There was a positive correlation between the expression of p53 and MGMT ($p = 0.08$). CONCLUSIONS: These preliminary findings suggest that for patients treated with FOLFIRINOX as a first-line treatment for metastatic pancreatic adenocarcinoma, the immunohistochemical evaluation of MGMT could not predict the clinical outcome; however, the survival was not significant probably because of the under-powered study (due to small sample size). A strong tumor expression of p53 is associated with a poor prognosis of OS.
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