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PD-L1 and PD-L2 expression after chemotherapy in metastatic gastric cancer

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Purpose: The effect of chemotherapy on programmed death ligand-1 (PD-L1) and PD-L2 expression is not fully understood. Therefore we aimed to investigate the effect of chemotherapy to PD-L1/2 expression in metastatic gastric cancer (mGC). **Methods:** We evaluated PD-L1 and 2 expression of 63 patients with paired tumor tissues before and after palliative first line platinum-based chemotherapy by using immunohistochemistry(IHC) method in each tumor specimens. **Results:** There was no significant difference in PD-L1 and PD-L2 expression between the clinicopathological parameters. The detection of PD-L1 on tumor cells decreased from 58% to 38% after chemotherapy ($p=0.028$), but showed no change with PD-L2 (from 43% to 36%). In patients with objective response (CR and PR), PD-L1 expression decreased with statistical significance ($p=0.033$), but not in patients with response of SD and PD ($p=0.275$).In univariate and multivariate analysis, patients with positive PD-L1 at the pre-chemotherapy showed better progression free survival (PFS, hazard ratio [HR]=0.42, $p=0.014$). In contrast, patients with positive post-chemotherapy PD-L1 showed decreased PFS (HR=1.97, $p=0.023$). And pre-chemotherapy PD-L1 statuses didn't have any correlation with OS difference, however, post-chemotherapy PD-L1 negative patients had prolonged OS (HR=1.92, $p=0.047$). PD-L2 statuses didn't show no difference of PFS and OS before and after chemotherapy. Univariate and Multivariate analysis showed that negative to positive conversion and positive to negative conversion of PD-L1 expression was associated with worse PFS (HR=0.030, $p=0.03$) and better PFS (HR=0.02, $p=0.024$), respectively. **Conclusions:** Our data suggests that chemotherapy may have an effect on the status of PD-L1 and PD-L2 expression. PD-L1 and PD-L2 expression may change during chemotherapy, so we suggest monitoring the pattern of change through serial tumor samples to reflect the correct status of PD-L1 expression.

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Comparison of HER2 status in primary gastric adenocarcinomas and corresponding malignant ascites

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Background: Peritoneal carcinomatosis appears to be the most common pattern of metastasis in gastric cancer patients and up to 40% have peritoneal spread causing ascites. The aim of this study was to compare human epidermal growth factor receptor 2 (HER2) status in primary gastric adenocarcinomas and corresponding cell blocks of malignant ascites. **Methods:** HER2 status was evaluated by immunohistochemistry (IHC) in primary gastric adenocarcinomas and paired cell blocks of malignant ascites in 44 patients. All cell blocks of malignant ascites from patients with gastric adenocarcinoma were confirmed by pathologic diagnosis. **Results:** HER2 expression was detected by IHC in 34.1% (15/44) of primary gastric adenocarcinomas and 20.5% (9/44) of cell blocks of malignant ascites. HER2 overexpression defined by IHC 3+ was observed in 4.5% (2/44) of primary gastric adenocarcinomas and 4.5% (2/44) of cell blocks of malignant ascites. However, all of these four patients exhibited discordant; two patients with HER2 overexpression in malignant ascites exhibited HER2 negativity in primary gastric adenocarcinomas, while two patients HER2 overexpression in primary gastric adenocarcinomas exhibited HER2 negativity in malignant ascites. Of the 13 patients with two or more serially sampled cell blocks of ascites, the IHC scores of four patients (30.8%) differed between each cell blocks of ascites. **Conclusions:** The incidence of HER2 overexpression is very low in patients with gastric adenocarcinoma and peritoneal carcinomatosis. HER2 status was discordant between primary gastric adenocarcinomas and malignant ascites or among serially sampled malignant ascites in a significant portion of gastric adenocarcinomas. The sensitivity of HER2 overexpression detection could be improved if both primary gastric adenocarcinomas and malignant ascites are used. Such testing enables optimized selection of HER2-targeted therapy-eligible patients in patients with advanced gastric cancer and malignant ascites.