Microarray-based response prediction in esophageal adenocarcinoma.

Abstract:
In locally advanced (uT3, N+)+ adenocarcinomas of the esophagus, neoadjuvant chemotherapy improves patient outcome. However, only a subgroup of patients responds. Therefore, in the present study, we evaluated whether the response to neoadjuvant chemotherapy can be predicted by a pretreatment tumor biopsy analysis. Biopsies of 47 patients with locally advanced (uT3, N+) adenocarcinoma of the esophagus were obtained during primary staging. All patients underwent neoadjuvant chemotherapy with cisplatin, 5-fluorouracil, and leucovorin and subsequent resection of the esophagus. Biopsies were used for microarray analysis. The predominance of tumor cells within the specimens was >70%. Affymetrix U133 plus 2.0 gene chips with 54675 probe sets were used. A statistical comparison of patients responding to chemotherapy versus nonresponding patients was done. All patients were examined with immunohistology against Ephrin B3 receptor and Ki-67. A total of 86 genes were at least 2-fold differentially regulated comparing responding with nonresponding adenocarcinomas of the esophagus. The predominant genes encoded for the regulation of the cell cycle, transduction, translation, cell-cell interaction, cytoskeleton, and the signal transduction. The strongest difference was seen for the Ephrin B3 receptor. This result could be confirmed by immunohistology. A statistical
significant correlation between the Ephrin B3 receptor, chemotherapy response, pathologic staging, and grading could be shown. There were significant differences in the gene profile between patients with adenocarcinoma of the esophagus responding to neoadjuvant chemotherapy compared with nonresponding patients. This suggests that it could be possible to characterize patients responding to chemotherapy even before starting the treatment using customized microarray analysis.