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Titel des Beitrags: Chromosomal instability rather than p53 mutation is associated with response to neoadjuvant cisplatin-based chemotherapy in gastric carcinoma.

Abstract: PURPOSE: The objective of the study was to evaluate microsatellite alterations [microsatellite instability (MSI) and loss of heterozygosity (LOH)] and mutation in the p53 gene in relation to response and patient survival to a cisplatin-based neoadjuvant chemotherapy in gastric cancer. EXPERIMENTAL DESIGN: Fifty-three pretherapeutic gastric carcinoma biopsies were analyzed with 11 microsatellite markers. The entire coding region of the p53 gene (exons 2-11) was analyzed for mutations by denaturing high-pressure liquid chromatography and sequencing. p53 protein expression was evaluated by immunohistochemistry. Patients were treated with a cisplatin-based, neoadjuvant chemotherapy regimen. Therapy response was evaluated by computed tomography scan, endoscopy, and endoluminal ultrasound. The median follow-up of the patients was 45.6 months. RESULTS: p53 mutations were identified in 19 of the 53 (36%) analyzed tumors. No significant association with response or survival was found for p53 mutation or for p53 protein expression. MSI (either high-grade MSI or low-grade MSI) did not show a correlation with response. With respect to LOH, LOH at chromosome 17p13 showed a significant association with therapy response (P = 0.022) but did not reach
statistical significance in terms of patient survival. The global LOH rate, expressed as fractional allelic loss (FAL), was assessed, and tumors were classified into tumors with a high (>0.5), medium (>0.25-0.5), and low (0-0.25) FAL value. A statistically significant association of FAL with therapy response was found (P = 0.003), with a high FAL being related to therapy response. The sensitivity, specificity, positive predictive value, and negative predictive value for FAL > 0.5 were 45%, 93%, 82%, and 72%, respectively. CONCLUSIONS: A high level of chromosomal instability (high FAL value) defines a subset of patients who are more likely to benefit from cisplatin-based neoadjuvant chemotherapy. p53 mutation status is not significantly associated with therapy response and is not a useful marker for response prediction.