Histone Deacetylase (HDAC) 1 and 2 Expression and Chemotherapy in Gastric Cancer.

Abstract: BACKGROUND: Histone deacetylases (HDACs) modulate chromatin and may influence the effect of DNA-damaging drugs. We investigated HDAC1 and -2 expression in gastric carcinomas (GCs) for an association of patient outcome with conventional neoadjuvant chemotherapy. In vitro, HDAC inhibitors were evaluated as alternative treatment options.

METHODS: HDAC1/2 expression was analyzed immunohistochemically in 127 pretherapeutic biopsy samples of neoadjuvant (platinum/5-fluorouracil) chemotherapy-treated GC patients and correlated with response and overall survival (OS). Chemosensitivity of four GC cell lines to cisplatin and the HDAC inhibitors suberoylanilide hydroxamic acid (SAHA) and valproic acid was determined by XTT assays. Efficiencies of combined drug schedules were analyzed. RESULTS: High expression of HDAC1/2 was found in 69 (54%) of 127 and 108 (85%) of 127 carcinomas, respectively, and was not associated with response or OS. In patients whose disease responded to therapy, high HDAC1 expression was associated with worse OS (P = 0.005). In cell lines, sequential treatment with SAHA and cisplatin showed synergistic effects irrespective of the initial cisplatin sensitivity.

CONCLUSIONS: HDAC1 and -2 expression is not suitable to predict response or survival for neoadjuvant-treated GC patients, but
HDAC1 expression may be used for risk stratification in patients whose disease responds to therapy. Sequential treatment with SAHA and cisplatin may represent an alternative treatment option for GC patients.