PURPOSE: Osteosarcoma, the most common primary malignant tumor of the bone, is characterized by complex karyotypes with numerous structural and numerical alterations. Despite attempts to establish molecular prognostic markers at the time of diagnosis, the most accepted predictive factor remains the histologic evaluation of necrosis after neoadjuvant chemotherapy. The present approach was carried out to search for genome-wide recurrent loss of heterozygosity and copy number variations that could have prognostic and therapeutic impact for osteosarcoma patients.

EXPERIMENTAL DESIGN: Pretherapeutic biopsy samples of 45 osteosarcoma patients were analyzed using Affymetrix 10K2 high-density single nucleotide polymorphism arrays. Numerical aberrations and allelic imbalances were correlated with the histologically assessed response to therapy and clinical follow-up.

RESULTS: The most frequent genomic alterations included amplifications of chromosome 6p21 (15.6%), 8q24 (15.6%, harboring MYC), and 12q14 (11.1%, harboring CDK4), as well as loss of heterozygosity of 10q21.1 (44.4%). All these aberrations and the total degree of heterozygosity of each tumor were significantly associated with an adverse outcome of patients and were used to define a chromosomal
alteration staging system with a superior predictive potential compared with the histologic regression grading. CONCLUSIONS: Structural chromosomal alterations detected by single nucleotide polymorphism analysis provide a simple but robust parameter to anticipate response to chemotherapy. The proposed chromosomal alteration staging system might therefore help to better predict the clinical course of osteosarcoma patients at the time of initial diagnosis and to adapt neoadjuvant treatment in patients resistant to the current protocols.