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PA-02. CORRELATIONS BETWEEN MULTIPLE MOLECULAR MARKERS' EXPRESSION AND SURVIVAL IN PATIENTS WITH GLIOBLASTOMA MULTIFORME TREATED WITH THE CURRENT STANDARD TREATMENT

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Glioblastoma multiforme (GBM) is an aggressive cancer. The median reported survival for patients with this disease is between 1 and 2 years. However, there is high heterogeneity in patients' response to treatment, disease-free survival, and overall survival (OS), which cannot be accurately predicted at the time of diagnosis. Moreover, most GBM studies have included patients that received different treatments, making it hard to extrapolate the data to the standard treatment. Our objective was to study the OS-predictive value of various molecular markers representing different pathways of oncogenesis in a group of patients with primary GBM that received the current standard of treatment. We identified 19 GBM patients who were treated in the KU Oncology Center between January 1, 2000, and July 30, 2004, with surgical resection followed by conformal radiation and temozolomide per Stupp. All patients but one continued on temozolomide until progression. The antibodies used targeted different pathways, such as proliferation (MIB-1), tumor progression and resistance to apoptotic signals (p53), cell migration and invasion (MMP2), control of cell cycle and transcriptional regulation (MAPK), proliferation (EGFR), angiogenesis (VEGF), and resistance to temozolomide (O-6–methylguanine DNA transferase). Both semiquantitative and quantitative (ACIS II, Clarient, San Juan Capistrano, CA, and ISI) methods were used to evaluate the immunostained sections, and these results were correlated to length of survival. The data were analyzed with PC-SAS software (SAS Institute, Cary NC) using stepwise logistic regression analysis for survival (defining trends for $P < 0.1$). The patients included in our study had a median age of 53 years (range, 29–71 years), a median performance score of 80% (range, 50–100%), and a mean survival of 601 days (range, 159–1,189 days). The only markers that showed trends toward correlating with increased survival were high p53 levels ($P = 0.07$) and low MAPK ($P = 0.08$), although low MMP2 was close to the threshold ($P = 0.14$). The other molecular markers, including EGFR, VEGF and MGMT, did not correlate with patient survival. Of the four patients who lived more than 30 months, all had negative EGFR staining, and three had negative p53 and very low or absent MGMT. This pilot study suggests that the most important pathways for tumor activity in patients treated with temozolomide are those involved in apoptosis (p53), cell cycle control (MAPK), and possibly local migration (MMP2). The ability to predict patient survival and response to treatment at the time of the initial diagnosis would be an invaluable tool both for planning future therapies and for patients' treatment and quality-of-life decisions. We will further test whether a panel of 10 molecular markers involved in different aspects of tumorigenesis can be used to achieve greater accuracy in predicting patients' long-term prognosis.